PRESS RELEASE

Ipsen presents the results of the first in-human study of a recombinant fast-acting neurotoxin (rBoNT-E) at TOXINS 2019

Safety, tolerability and pharmacodynamics of BoNT-E demonstrated in Phase I study[1]

Paris (France), 17 January 2019 – Results of the first in-human study of a recombinant neurotoxin are being presented at the TOXINS International Conference in Copenhagen. Ipsen's recombinant BoNT serotype E (rBoNT-E) was investigated in a phase I study that demonstrated its safety and tolerability profile in healthy volunteers[1]. The study also reported that it has a faster onset of action and a shorter duration of effect, as well as a quick time to peak activity, in comparison with established BoNT-A products. Further studies will be initiated to establish potential aesthetic and therapeutic uses of this investigational therapy.

"The application of recombinant techniques to create novel botulinum toxin-based medicines with different onsets and durations of action, will potentially offer clinicians the flexibility to choose the most appropriate neurotoxin for each patient, which is not an option today," said **Philippe Picaut, Pharm. D., PhD, Senior Vice President Research & Development for the Neuroscience Therapeutic Area, Ipsen**.

Botulinum neurotoxins (BoNTs) are naturally occurring proteins (produced by *Clostridium* bacteria) that were first discovered in the 19th century. They are classified into seven serotypes (A-G) with the majority of commercialized BoNT products being serotype A. BoNTs are used in multiple different conditions after injection in skeletal muscles (eg cervical dystonia, hemifascial spasm, blepharospasm, spasticity in adult and children; aesthetic); smooth muscles (neurogenic detrusor overactivity, idiopathic bladder overactivity) or exocrine gland hyperfunction (eg sialorrhea, axillary hyperhidrosis).

Alexandre Lebeaut, M.D., Executive Vice President, Research & Development and Chief Scientific Officer, Ipsen stated: *"Neurotoxin research is advancing at an unprecedented rate and we, at Ipsen, are at the forefront of this transformation, developing innovative therapeutic and aesthetic solutions that help patients take back control of their lives".*

Ipsen will have 50 posters at Toxins 2019 in Copenhagen, including:

- 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.
- New modified recombinant botulinum neurotoxin type F with enhanced potency; Burgina et al.

About the study[1]

This was a randomised, double-blind, placebo-controlled study, performed in male healthy volunteers at a single study centre in the UK (EudraCT: 2016-002609-20). Participants were healthy males (aged 18–49 years), who had not previously been treated with BoNT (any serotype) during the past 6 months. Overall, 65 subjects were screened and 28 were randomised to receive rBoNT-E or placebo (21 versus 7, respectively).

Subjects provided written informed consent prior to any study-related procedure and could withdraw at any time for any reason.

A baseline Extensor Digitorum Brevis CMAP total amplitude (peak-to-peak) ≥5 mV during electrophysiological examinations at screening and before study drug administration was required. Overall, rBoNT-E was well tolerated at the assessed doses. The majority of TEAEs were considered unrelated to treatment. There was no local diffusion to adjacent muscles for rBoNT-E at any dose level and no subject seroconverted following rBoNT-E injection.

References

1. Field, M. *et al.* AbobotulinumtoxinA (Dysport®), OnabotulinumtoxinA (Botox®), and IncobotulinumtoxinA (Xeomin®) Neurotoxin Content and Potential Implications for Duration of Response in Patients. *Toxins (Basel).* **10,** 535 (2018).

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 Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipsen.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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