PRESS RELEASE

Ipsen demonstrates continued commitment to rare diseases with eight abstracts accepted at ENDO 2020 published in the *Journal of the Endocrine Society*

Data published evaluates fibrodysplasia ossificans progressiva (FOP) natural disease progression

The Natural History Study (NHS) is the first protocol-specified, longitudinal evaluation of FOP disease progression

PARIS, FRANCE, 08 June 2020 – Ipsen (Euronext: IPN; ADR: IPSEY), shared data from the company's growing Rare Diseases Therapeutic Area, with the publication of eight abstracts in the *Journal of the Endocrine Society*. The data include a first-of-its kind study titled, "A Natural History Study of Fibrodysplasia Ossificans Progressiva (FOP): 12-Month Outcomes," highlighting one-year data on the natural progression of FOP and the impact of heterotopic ossification (HO) on patients' physical functioning over time.[1] Ipsen and its partners also shared several studies detailing findings from health economics and outcomes research on the management of acromegaly.

FOP is an ultra-rare, severely disabling genetic bone disease that affects approximately 1.36 per million individuals worldwide.[2,3] FOP is characterized by formation of bone in soft and connective tissues, known as heterotopic ossification (HO).[4] Sporadic episodes of painful soft tissue swelling called 'flare-ups' can precede HO.[4] HO is permanent, cumulative and severely impacts physical function over time with most patients' movement becoming extremely limited, often confining them to a wheelchair by their twenties.[4]

The prospective Natural History Study (NHS) of FOP is the first global, multicenter, longitudinal study designed to measure disease progression over three years.[1] Participant selection was representative of the FOP community worldwide and includes 114 patients with FOP who harbor a documented ACVR1 mutation, of those 99 (55 male / 44 female; mean age of group: 17.4 years) had both baseline and 12-month assessments and were included in the analysis. Ninety-three of the 99 participants had evaluable whole-body computed tomography and were included in the HO analysis.[1]

The analysis showed that over the course of 12 months, 40% (37/93) of participants had new HO.[1] Of the NHS participants with new HO, 65% (24/37) reported at least one flare-up (mean rate of 2.3 flare-ups/year).[1] 60% (56/93) of NHS participants did not experience new HO over 12 months.[1] Of those participants, 43% (24/56) reported at least one flare-up (mean rate of 1.8 flare-ups/year).[1] CAJIS and FOP-PFQ were not sufficiently sensitive to assess FOP disease progression over 12 months.

"The results show that evaluating HO may be a viable way to measure disease progression and potential treatment effect," said study co-investigator and co-author, Mona Al Mukaddam, M.D., MS of the Center for Research in FOP and Related Disorders, Perelman School of Medicine, University of Pennsylvania. "By examining the natural course of FOP, we hope to better understand the physical burden of HO as well as the link between flare-ups and disease progression."

Additional abstracts published in the *Journal of the Endocrine Society* included data on the management of patients living with FOP or acromegaly.[5-11]

"Our research reinforces Ipsen's commitment to actively listen to and work with patients, physicians, nurses, patient association groups, and other key stakeholders to best address the complexity and challenges of living with rare diseases such as FOP or acromegaly," said Jim Roach, M.D., Senior Vice President and Global Head, Rare Diseases Therapeutic Area at Ipsen. "These diseases impact the quality of life both for patients and their caregivers and often place economic and societal burdens due to absences from work and high healthcare costs. Enhancing our understanding of these diseases will hopefully allow us to develop solutions that meaningfully impact patients."

Overview of Ipsen data accepted by ENDO 2020:

Medicine/Disease	Abstract Number/Title	Study Authors
FOP	OR29-05 - A Natural History Study of Fibrodysplasia Ossificans Progressiva (FOP): 12-Month Outcomes[1]	Mona Al Mukaddam, Robert J. Pignolo, Geneviève Baujat, Matthew A. Brown, Carmen De Cunto, Maja Di Rocco, Edward C. Hsiao, Richard W. Keen, Kim-Hanh Le Quan Sang, Andrew Strahs, Rose Marino, and Frederick S. Kaplan
	SUN-344 - Patients with Fibrodysplasia Ossificans Progressiva Have an Increased Prevalence of Cardiac Conduction Abnormalities[5]	Samuel Kou, Carmen De Cunto, Geneviève Baujat, Kelly L. Wentworth, Donna Grogan, Matthew A. Brown, Maja Di Rocco, Richard Keen, Mona Al Mukaddam, Frederick S. Kaplan, Robert J. Pignolo, and Edward C. Hsiao
Palovarotene	MON-348 - Surgical Management of Bilateral Hip Fracture in a Patient with Fibrodysplasia Ossificans Progressiva Treated with Palovarotene[6]	Sukhmani Singh, Joseph Kidane, Kelly L. Wentworth, Daria Motamedi, Saam Morshed, and Edward C. Hsiao
Acromegaly	SUN-296 - Acromegaly Significantly Impacts Employees' Health Benefit Costs and Increases Work Absenteeism[7]	Kevin C.J. Yuen, Kathryn A. Munoz, Richard Alan Brook, John D. Whalen, Ian A. Beren, and Antonio Ribeiro-Oliveira
	MON-141 - Healthcare Services Utilization and Costs Associated with the Management of Patients Living with Acromegaly[8]	Antonio Ribeiro-Oliveira, Kathryn A. Munoz, Richard Alan Brook, Ian A. Beren, John D. Whalen, and Kevin C.J. Yuen
	MON-306 - Acromegaly Comorbidity Costs, Quality of Life, and Mortality: Lifetime Comparisons for Controlled Acromegaly, Uncontrolled Acromegaly, and the General US Population[9]	Melanie D. Whittington, Jonathan D. Campbell, R. Brett McQueen, Kathryn A. Munoz, John D. Whalen, and Antonio Ribeiro-Oliveira
Somatuline® Autogel/Depot	MON-301 - Long-Acting SSA Treatment Patterns in Sweden From 2005 to 2017: A Nationwide Study[10]	Daniel S. Olsson, Daniel Granfeldt, Åse Björstad, Antonio Ribeiro-Oliveira, Anna Jonasson, John D. Whalen
	MON-LB47 - An International Simulated Use Study (PRESTO) to Evaluate Nurse Preferences Between the Lanreotide Autogel New Syringe and Octreotide Long-Acting Release Syringe[11]	Daphne T. Adelman, Xuan-Mai Truong-Thanh, Marion Feuilly, Aude Houchard, and David Cella

About fibrodysplasia ossificans progressiva (FOP)

Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare, severely disabling disorder characterized by progressive heterotopic ossification (HO), or the abnormal transformation of muscle, ligaments and tendons into bone.[4] HO may be spontaneous or associated with painful episodic disease flare-ups that are usually precipitated by soft tissue injury.[4] As the disease progresses, extra-skeletal bone increasingly restricts joints, resulting in severe disability and loss of mobility, compromised respiratory function and increased risk of early death.[4] FOP

is caused by a mutation in the gene for ALK2, which is known as ACVR1, leading to inappropriate activation of the bone morphogenetic pathway.[4] FOP is among the rarest of human diseases, and while there are approximately 1,000 described cases globally, the prevalence of FOP is estimated at approximately 1.36 per million individuals.[2,3]

About Acromegaly
Acromegaly is a rare, chronic pituitary hormonal disorder with physical, neuropsychiatric and neurocognitive symptoms. Due to the insidious onset, slow progression and lack of awareness of the disease, acromegaly often takes 5-10 years to diagnose. Diagnostic delays can lead to an increased number and more severe symptoms and comorbidities that can become difficult to manage, reduce the quality of life and increase the risk of mortality.[12] It is usually caused by having too much growth hormone in the body which, over time, results in some characteristic symptoms and signs, such as heavy or prominent facial features with a prominent jaw line and enlarged hands and feet.[12]

About palovarotene
Palovarotene is a RARγ agonist being developed as a potential treatment for patients with ultra-rare and debilitating bone diseases, including fibrodysplasia ossificans progressiva (FOP) and multiple osteochondromas (MO), as well as other conditions including dry eye disease. Palovarotene, which had rare pediatric disease and breakthrough therapy designations for the treatment of an ultra-rare bone disorder, was acquired by Ipsen through the acquisition in April 2019 of Clementia Pharmaceuticals.

About Somatuline® (lanreotide)
Somatuline® Autogel® is made of the active substance lanreotide, which is a somatostatin analogue that inhibits the secretion of growth hormone and certain hormones secreted by the digestive system. The main indications of Somatuline® and Somatuline® Autogel® are:[13]

- The treatment of individuals with acromegaly when the circulating levels of Growth Hormone (GH) and/or Insulin-like Growth Factor-1 (IGF-1) remain abnormal after surgery and/or radiotherapy, or in patients who otherwise require medical treatment.
- The treatment of grade 1 and a subset of grade 2 (Ki-67 index up to 10%) gastroenteropancreatic neuroendocrine tumors (GEP-NETs) of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease.
- The treatment of symptoms associated with neuroendocrine (particularly carcinoid) tumors.

Important Safety Information
The detailed recommendations for the use of Somatuline® Autogel® are described in the Summary of Product Characteristics (SmPC), available here.

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, 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 €2.5 billion in 2019, 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 5,800 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

Ipsen's 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, and the outcome of this study or other studies. 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 preclinical 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 6 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 2019 Registration Document available on its website (www.ipsen.com).

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