This press release has been approved by ASBMR for distribution on 25 August

PRESS RELEASE

Ipsen to present results from MOVE, the first global Phase III trial in fibrodysplasia ossificans progressiva (FOP), at ASBMR 2020 annual meeting

- Post hoc analyses showed substantial reduction (62%) in mean annualized new heterotopic ossification volume in patients with FOP who were treated with oral investigational therapy palovarotene[1]

- Results from the third interim analysis of the MOVE trial, the first and only multicenter Phase III study of its kind, comprising the largest interventional study in FOP to date with 107 participants, suggest that palovarotene may be an important therapeutic option in FOP[1]

PARIS, FRANCE, 25 August 2020 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced results from the MOVE trial, the first and only multicenter Phase III study in fibrodysplasia ossificans progressiva (FOP), to be presented during an oral presentation at the American Society for Bone and Mineral Research (ASBMR) 2020 annual meeting (Saturday, 12 September, 11:00am - 12:30pm ET). Dosing of palovarotene in the MOVE clinical trial was paused when futility criteria were met at a pre-specified interim analysis. However, subsequent post hoc analyses showed the RARγ agonist oral investigational therapy palovarotene reduced mean annualized new heterotopic ossification (HO) volume in pediatric and adult participants with FOP. This was compared with untreated patients from a natural history study over 24 months.[1]

Results from the MOVE trial demonstrated a 62% reduction in mean annualized new HO volume in participants treated with palovarotene (8,821 mm^3) (n=97) versus untreated (23,318 mm^3) (n=98) patients (nominal weighted linear mixed effects [wLME] model est. –11,611mm^3, p-value = 0.0292). Premature physeal closure (PPC) (n=18) or epiphyseal disorder (n=1) was observed in 27.1% (19/70) of participants who were skeletally immature at baseline.[1] Palovarotene safety data were otherwise generally consistent with the known adverse event (AE) profile of retinoids.

FOP is an ultra-rare, genetic disorder that affects approximately 1.36 per million individuals worldwide[2,3] and is characterized by formation of bone in soft and connective tissues, known as HO.[4] Sporadic episodes of painful soft tissue swelling, called "flare-ups", can precede HO.[3] HO is permanent and leads to severe functional limitations in joint mobility, progressive and cumulative disability and to shortened life expectancy. There are currently no approved treatments for the reduction or prevention of heterotopic bone formation in FOP.[4]

"Accumulation of HO across the body is the defining characteristic of FOP and severely limits physical function over time," said Dr Robert Pignolo, M.D., Ph.D., Division of Geriatric Medicine and Gerontology, Department of Internal Medicine, Mayo Clinic. "The MOVE trial provides important insight into long-awaited treatment strategies and demonstrates that the oral therapy palovarotene can reduce new HO volume, representing an important therapeutic option in FOP especially in older children and adults."

"We are pleased to present the third interim analysis results of the Phase III MOVE trial in FOP, evaluating Ipsen's oral investigational therapy palovarotene, to the global community at the ASBMR annual meeting," said Jim Roach, M.D., Senior Vice President and Global Head of Rare Diseases Therapeutic Area at Ipsen. "Based on preliminary discussions with the FDA, Ipsen's intent is to move forward with an NDA submission and discussions with the EMA are ongoing. We remain committed to working with regulators and are delighted to be one step closer to our goal of bringing this potential treatment option to people living with FOP in a timely manner."

"People living with FOP face life-threatening challenges with limited treatment options. We are encouraged by these data showing a reduction in HO volume from the MOVE trial, which hopefully will result in a new potential treatment option for the FOP community," said Adam Sherman of the International Fibrodysplasia Ossificans Progressiva Association (IFOPA).

MOVE (NCT03312634) is an ongoing Phase III, multicenter, open-label trial of 107 patients with FOP who received oral palovarotene as a chronic (5mg once daily) and episodic (20mg once daily for 4 weeks, followed by 10mg for ≥8 weeks for flare-ups and trauma) regimen. The primary objectives of the MOVE trial are to evaluate the efficacy of palovarotene in reducing new HO volume in patients with FOP as assessed by low-dose, whole body computed tomography (WBCT, excluding head) compared with untreated patients from Ipsen's global FOP natural history study (NHS; NCT02322255), and to evaluate the safety of palovarotene in adult and pediatric patients with FOP.[5] The NHS is a first-of-its kind study into the evaluation of FOP disease progression. In June, Ipsen presented 8 abstracts in the Journal of Endocrine Society as part of our ongoing commitment to rare diseases. The data included an abstract highlighting 12-month data on the natural progression of FOP and the impact of HO on patients' physical functioning over time from the NHS study.[6]

At data cut off, all study participants had reported ≥1 treatment-emergent adverse event (TEAE); 97.0% reported ≥1 retinoid-associated TEAE (e.g. mucocutaneous events). Maximum AE severity was mild in 32.2% of participants, moderate in 45.5%, and severe in 22.2%. Premature physeal closure (PPC) (n=18) or epiphyseal disorder (n=1) was observed in 27.1% (19/70) of participants who were skeletally immature at baseline.[1] Results demonstrated a 62% reduction in mean annualized new HO volume in participants dosed with palovarotene (8,821 mm^3) versus untreated (23,318 mm^3) patients (nominal wLME model p-value = 0.0292). The data presented on 12 September are from the third interim analysis (IA3) of MOVE.

About the FOP clinical program
The Phase III MOVE (NCT03312634) trial is an open-label, single-arm, efficacy and safety trial evaluating a chronic/episodic dosing regimen of palovarotene, which includes a chronic 5mg daily dose of palovarotene in addition to the episodic 20/10mg dosing regimen following flare-ups (weight-adjusted for skeletally immature participants). The trial is being conducted in Argentina, Australia, Brazil, Canada, France, Italy, Japan, Spain, Sweden, the United Kingdom, and the United States.[5] There are two ongoing Phase II (PVO-1A-202 [NCT02279095] and PVO-1A-204 [NCT02979769]) extension trials: 1) Study 202, an open-label extension of Study 201, the initial Phase II randomized, double-blind, multicenter trial; and 2) Study 204 an open-label trial to evaluate the safety and efficacy of different palovarotene dosing regimens in patients with FOP in France.

In December 2019 a partial clinical hold was applied to the pediatric population (participants under the age of 14 years) currently participating in the Phase II (PVO-1A-202/204 and PVO-2A-201) and Phase III (PVO-1A-301) studies in all clinical sites at global level. Subsequently a decision to pause dosing of palovarotene in all participants in the global Phase III MOVE trial (PVO-1A-301), as well as the ongoing Phase II (PVO-1A-202/204) extension studies in FOP was made by Ipsen on 24 January 2020, based on results of a futility analysis as part of the pre-specified interim analysis (Bayesian compound Poisson analysis with square root transformation of the new HO volume data). Encouraging therapeutic activity was observed in post hoc analyses of interim data for the Phase III MOVE trial and shared with, and acknowledged by, the Independent Data Monitoring Committee (IDMC). Post hoc analyses included Bayesian compound Poisson analysis without square root transformation, and weighted linear mixed effects models (with/without square root transformation of the new HO volume data). As such, the company amended the protocol for the Phase III MOVE trial to include updates to the statistical analysis section, including additional analyses requested by the IDMC, to be performed in addition to the primary pre-specified analysis. The protocol amendments are based on the IDMC's observation that the protocol pre-specified statistical model may have negatively affected the efficacy analysis and appears to have shifted the statistical conclusion from significant therapeutic benefit to showing futility of the treatment. Dosing for eligible study patients ≥14 years of age has resumed across the Phase II and Phase III programs for palovarotene in FOP.

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

About fibrodysplasia ossificans progressiva (FOP)
Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare, genetic disorder characterized by bone that forms outside the normal skeleton, in muscles, tendons, or soft tissue.[4] FOP is among the rarest of human diseases, and while there are approximately 1,000 described cases globally, the reported prevalence of FOP is estimated at approximately 1.36 per million individuals.[2,3]

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. 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 Universal Registration Document available on its website (www.ipsen.com).

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