

Ipsen provides update on palovarotene clinical programs

Ipsen to reinstate palovarotene dosing in patients 14 years of age and older with fibrodysplasia ossificans progressiva

Ipsen to terminate MO-Ped trial (PVO-2A-201) in patients with multiple osteochondromas to analyze accumulated data and assess the future of palovarotene in this indication

PARIS, France, 26 March 2020 — Ipsen (Euronext: IPN; ADR: IPSEY) announced today it will begin to reinstate palovarotene dosing in patients 14 years of age and older currently participating in its fibrodysplasia ossificans progressiva (FOP) clinical program. The Food and Drug Administration (FDA) in the U.S. has confirmed they have no safety concerns with restarting dosing in patients 14 years of age and older. Clearance to reinstate dosing in these patients has also been received to date from the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK, the National Agency for the Safety of Medicines and Health Products Safety (ANSM) in France, the Medical Products Agency (MPA) in Sweden, the Italian Medicines Agency (AIFA), the National Administration of Drugs, Foods, and Medical Devices (ANMAT) in Argentina, the Spanish Agency of Medicines and Medical Devices (AEMPS), and Health Canada (HC).

The decision to pause dosing of palovarotene 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.

Encouraging therapeutic activity was observed in preliminary post-hoc analyses of interim data for the Phase III MOVE trial and shared with, and acknowledged by, the Independent Data Monitoring Committee (IDMC). As such, the company amended the protocol for the Phase III MOVE trial to include updates to the statistical analysis section as recommended by the IDMC to allow for additional analyses 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 shifted the statistical conclusion from significant therapeutic benefit to showing futility of the treatment.

"We are pleased that Ipsen has received the approval to reinstate dosing in patients 14 years of age and older in the Phase III MOVE trial from several regulatory agencies to date following review of the additional data. After consultation with patient groups and investigators, we have been working diligently with all relevant stakeholders to restart the trial as quickly as possible," said Dr. Howard Mayer, Executive Vice President and Head of Research and Development at Ipsen. "We remain committed to bringing palovarotene to patients living with this devastating disease and will continue our conversations with the health authorities to determine the most appropriate regulatory path forward."

Ipsen is now working to obtain the approvals from the ethics committee (EC) of each clinical site and, upon receipt of both regulatory approval where required and EC approval, the reinstatement of dosing may begin. At this point, physicians or trial coordinators will contact eligible patients to share more details and advise on appropriate steps for the reinstatement of treatment. Appropriate measures will also be taken to ensure the safety of FOP patients who restart dosing in light of the ongoing COVID-19 pandemic, taking into consideration local regulatory and health authority guidance, as well as the ability of individual investigators and sites to adequately monitor patient safety.

The FDA partial clinical hold issued on 4 December 2019 for the pediatric population under the age of 14 for FOP and multiple osteochondroma (MO) studies remains in effect. In relation to this, Ipsen is currently addressing the questions from the FDA and other health authorities to expeditiously establish a course of action for FOP studies for the pediatric population under the age of 14.

Ipsen is also addressing the partial clinical hold questions from the FDA related to the MO program. However, Ipsen has taken the decision to terminate its MO-Ped trial (PVO-2A-201) conducted under IND135403 to analyze the accumulated data to better inform on the efficacy, safety and future of palovarotene in MO, and to potentially establish a path forward for palovarotene in this indication, including an assessment as to the potential for an NDA submission to the FDA. Ipsen believes however that an NDA submission for the treatment of MO based on the MO-Ped trial (PVO-2A-201) conducted under IND135403 is highly unlikely. The reasons for Ipsen's decision include the time that the partial clinical hold has been in place leading to a significant gap in dosing which may compromise the integrity of the data, that the trial was not fully enrolled at the time the partial clinical hold was instituted (as such, very few patients had reached the trial midpoint), and there is no efficacy data available in this patient population currently to further inform a benefit/risk assessment.

About the FOP clinical program

The Phase III MOVE (PVO-1A-301) trial is an open-label, single-arm, efficacy and safety trial evaluating a chronic/episodic dosing regimen of palovarotene which includes a 5 mg daily dose of palovarotene in addition to the episodic 20/10 mg dosing regimen following any flare-ups (note that doses are weight-adjusted). The trial is being conducted in the U.S., Argentina, Australia, Brazil, Canada, France, Italy, Japan, Spain, Sweden and the United Kingdom. There are two ongoing Phase II (PVO-1A-202/204) extension studies; 1) Study 202 an open-label extension of Study 201, the initial Phase II randomized, double-blind, multi-center trial, and 2) Study 204 an open-label study corresponding to PVO-1A-202 to evaluate the safety and efficacy of different palovarotene dosing regimens in subjects with FOP in France.

About palovarotene

Palovarotene is a RAR γ 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 fibrodysplasia ossificans progressiva (FOP)

Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare, severely disabling disorder characterized by bone that forms outside the normal skeleton, in muscles, tendons or soft tissue.¹ FOP is among the rarest of human diseases, and while there are approximately 1,000 confirmed cases globally, the 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. 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.ipсен.com.

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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 and also taking into consideration assessment delays of certain clinical trials in light of the ongoing COVID-19 pandemic. 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 2018 Registration Document available on its website (www.ipsen.com).

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