PRESS RELEASE

Ipsen receives CHMP negative opinion for palovarotene as a treatment for fibrodysplasia ossificans progressiva in E.U.

- Ipsen to request re-examination of CHMP opinion on palovarotene as a potential treatment for fibrodysplasia ossificans progressiva in E.U.
- FOP is an ultra-rare disease that continuously and permanently causes abnormal bone formation.[1] There are currently no disease-modifying treatment options available in E.U.
- Regulatory processes are continuing in other countries including the U.S.

PARIS, FRANCE, 27 January 2023 – Ipsen (Euronext: IPN; ADR: IPSEY) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended not to grant marketing authorization for investigational palovarotene as a treatment for the ultra-rare bone disease, fibrodysplasia ossificans progressiva (FOP). In the E.U. there are currently only symptomatic treatments for FOP, which do not reduce the formation of extra-skeletal bone in patients with the condition. Ipsen will be requesting a re-examination of the CHMP opinion, based on scientific data available from the existing palovarotene clinical trial program.

FOP causes permanent and continuous new bone formation in soft and connective tissues, like muscles, tendons and ligaments, a process known as heterotopic ossification (HO).[1] Once formed, it is irreversible.[1] The average age of diagnosis is 5 years old[2] and ultimately FOP shortens the median life expectancy to 56 years as untimely death is caused by bone formation around the ribcage leading to breathing problems and cardiorespiratory failure.[3] FOP has an estimated prevalence of 1.36 per million individuals and about 900 people are diagnosed worldwide; however, the number of confirmed cases varies by country.[4,5,6]

“We are disappointed with this outcome and will be requesting a re-examination of the CHMP opinion,” said Howard Mayer, Executive Vice President and Head of Research and Development for Ipsen. “We continue to work closely with the EMA to address the outstanding concerns that led to the decision today, with the goal of making this investigational medicine available to appropriate patients, living with this debilitating disease, where no other treatment option exists. Ipsen remains committed to bringing new therapeutic options to the FOP community, which has been instrumental in the development of investigational palovarotene through their involvement in clinical trials. We are enormously grateful for their continued support.”

The CHMP opinion is based on its review of data from MOVE, the first and largest Phase III efficacy and safety trial conducted in FOP. The primary objectives of MOVE were to evaluate the efficacy of palovarotene in reducing new HO volume, as assessed using whole-body computed tomography, compared with patients untreated beyond standard of care from Ipsen’s global FOP natural history study, and to evaluate the safety of investigational palovarotene in adult and pediatric patients with FOP.[7,8]

“There is a significant need for a treatment specifically developed to help manage the progression of this disease. The data from MOVE have helped us to understand the potential for treatments that reduce HO progression to be used in the management of FOP.” Said Dr. Genevieve Baujat, Clinical Geneticist Consultant at Necker-Enfants Malades Hospital, Paris, France. “Currently, the only therapeutic options available to us are for treating symptoms. We in the FOP community have been waiting a long time for innovations to treat this disabling disease.”

ENDS

About palovarotene

Palovarotene is an investigational oral medicine that selectively targets the retinoic-acid receptor gamma (RARγ), which is an important regulator of skeletal development and ectopic bone in the retinoid signaling pathway. Palovarotene is designed to mediate the interactions between the receptors, growth factors and proteins within the retinoid signaling pathway to reduce new abnormal bone formation (HO). Palovarotene received Orphan Drug and Breakthrough Therapy Designations from the U.S. Food and Drug Administration (FDA) for the potential treatment of FOP and was granted Priority Review. Palovarotene was also granted orphan medicine designation by the European Medicines Agency (EMA). Palovarotene is in review processes with a number of regulatory authorities including the FDA and the EMA. Palovarotene is currently authorized for use in appropriate patients in Canada and provisionally in the U.A.E. where it is marketed as Sohonos™ (palovarotene capsules).[9,10]

About the MOVE trial

MOVE (NCT03312634) is a Phase III, multicenter, single-arm, open-label trial to assess the efficacy and safety of palovarotene. 107 study participants with FOP 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 endpoint was annualized change in new HO volume measured by low-dose whole-body computed tomography. Efficacy data from participants enrolled in MOVE were compared with data from FOP Natural History Study (NHS) participants untreated beyond standard of care; individuals ≤65 years of age with clinically diagnosed FOP and a verified ACVR1R206H pathogenic variant were eligible for inclusion in the NHS.[7]

About Ipsen

Ipsen is a global, mid-sized biopharmaceutical company focused on transformative medicines in Oncology, Rare Disease and Neuroscience. With Specialty Care sales of €2.6bn in FY 2021, Ipsen sells medicines in over 100 countries. Alongside its external-innovation strategy, the Company's research and development efforts are focused on its innovative and differentiated technological platforms located in the heart of leading biotechnological and life-science hubs: Paris-Saclay, France; Oxford, U.K.; Cambridge, U.S.; Shanghai, China. Ipsen has around 5,000 colleagues worldwide and is listed in Paris (Euronext: IPN) and in the U.S. through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information, visit ipsen.com

For further information:

Contacts

Investors

Craig Marks
Vice President, Investor Relations
+44 (0)7584 349 193

Adrien Dupin de Saint-Cyr
Investor Relations Manager
+33 6 64 26 17 49

Media

Anna Gibbins
Global Head of Franchise Communications, Rare Disease
+44 (0)7717 801 900

Ipsen's Forward-Looking Statements

The forward-looking statements, objectives and targets contained herein are based on Ipsen'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 Ipsen'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 Ipsen'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 Ipsen. 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 medicine 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. Ipsen must face or might face competition from generic medicine 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 Ipsen may fail to achieve its objectives and be forced to abandon its efforts with regards to a medicine in which it has invested significant sums. Therefore, Ipsen 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 medicine concerned. There can be no guarantees a medicine will receive the necessary regulatory approvals or that the medicine 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 healthcare legislation; global trends toward healthcare cost containment; technological advances, new medicine and patents attained by competitors; challenges inherent in new-medicine development, including obtaining regulatory approval; Ipsen'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 Ipsen's patents and other protections for innovative medicines; and the exposure to litigation, including patent litigation, and/or regulatory actions. Ipsen also depends on third parties to develop and market some of its medicines which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to Ipsen's activities and financial results. Ipsen 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 Ipsen's partners could generate lower revenues than expected. Such situations could have a negative impact on Ipsen's business, financial position or performance. Ipsen 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. Ipsen'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 Ipsen's 2021 Universal Registration Document, available on ipsen.com

[1] Kaplan FS et al. The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. *Proc Intl Clin Council FOP.* 2019;1:1-111.
[2] Pignolo RJ et al. The Natural History of Flare-Ups in Fibrodysplasia Ossificans Progressiva (FOP): A Comprehensive Global Assessment. *J Bone Miner Res*. 2016;31(3):650-656.
[3] Kaplan FS, Zasloff MA, Kitterman JA et al. Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva, *J Bone Joint Surg Am.* 2010;92(3):686-691.
[4] Baujat et al. Prevalence of fibrodysplasia ossificans progressiva (FOP) in France: an estimate based on a record linkage of two national databases. *Orphanet J Rare Dis*. 2017;12:123.
[5] IFOPA, What is FOP?, *IFOPA*. Viewed 30 November 2022. <https://www.ifopa.org/what_is_fop>.
[6] Lilijesthrom M, Pignolo RJ, Kaplan FS. Epidemiology of the global fibrodysplasia ossificans progressiva (FOP) community. *J Rare Dis Res Treat.* 2020;5(2):31-36.

[7] Pignolo RJ, Hsiao E, Al Mukaddam M et al. Reduction of New HO in the Open-Label, Phase 3 MOVE Trial of Palovarotene for Fibrodysplasia Ossificans Progressiva (FOP). *J Bone Miner Res.* 2022.
[8] Pignolo RJ, Baujat G, Brown M et al. The natural history of fibrodysplasia ossificans progressiva: A prospective 36-month study. Gen Med. 2022,ISSN 1098-3600,https://doi.org/10.1016/j.gim.2022.08.013.
[9] Government of Canada, Notice: Multiple Additions to the Prescription Drug List (PDL). Viewed 30 November 2022, <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/prescription-drug-list/notices-changes/multiple-additions-2022-01-24.html>.
[10] Ipsen data on file.