Disclaimer: Intended for international media and investor audiences only

PRESS RELEASE

Ipsen confirms U.S. FDA accepts New Drug Application for palovarotene as the first potential treatment worldwide for fibrodysplasia ossificans progressiva (FOP)

- New Drug Application granted Priority Review status, with a decision anticipated on 30 November 2021
- European Medicines Agency (EMA) and Swissmedic have also validated the Marketing Authorization Application (MAA) for palovarotene with Swissmedic granting palovarotene a priority review

PARIS, FRANCE, 28 May 2021 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that its New Drug Application (NDA) for palovarotene, an oral, investigational, selective RARγ agonist for the prevention of heterotopic ossification (new bone formation) as a potential treatment option for people living with the progressive disabling and ultra-rare genetic disorder fibrodysplasia ossificans progressiva (FOP), has been accepted by the U.S. Food and Drug Administration (FDA). The target regulatory action date assigned by the FDA under a Priority Review status is 30 November 2021.

FOP is an ultra-rare genetic disorder with an estimated prevalence of 1.36 per million individuals; however, the number of confirmed cases varies by country.[1,2] It is characterized by new bone formation outside of the normal skeletal system, like in soft connective tissues, a process known as heterotopic ossification (HO),[3] which can be preceded by painful soft-tissue swelling or "flare-ups".[2] Flare-up episodes are common and are a substantial contributor to the formation of new HO, however HO can form in the absence of a flare-up. HO, once formed, is irreversible and leads to loss of mobility and shortened life expectancy.[3]

Dr. Howard Mayer, Executive Vice President and Head of Research and Development, Ipsen, said "With no approved treatments for this progressive and debilitating disease, there remains a great unmet medical need for the FOP community. This year marks 15 years since the discovery of the mutation in the gene *ALK2/ACVR1* which causes FOP, and the palovarotene submission is the first worldwide for a potential treatment in this disease. Our teams at Ipsen are now focused on working closely with regulatory authorities to bring this potential treatment option to people living with FOP around the world. We want to thank all the people living with FOP, their families, caregivers and healthcare teams who have participated in the palovarotene clinical program."

The NDA for palovarotene is primarily based on data from the ongoing MOVE trial, the first global multi-center Phase III trial in FOP. MOVE is an open-label, single-arm trial, evaluating the efficacy and safety of a chronic/flare-up dosing regimen of palovarotene in decreasing new annualized HO volume in patients with FOP. Post hoc analyses* of the primary endpoint from the trial demonstrated a 62% reduction in mean annualized new HO volume in participants treated with palovarotene (8,821 mm^3) (n=97) versus untreated participants from a natural-history study (23,318 mm^3) (n=98) (nominal weighted linear mixed effects [wLME] model est. –11,611mm^3, p-value = 0.0292). Overall, 29.3% of participants reported at least one serious adverse event (AE), including premature physeal closure (PPC) or epiphyseal disorder in 27.1% of the participants who were skeletally immature at baseline.[4] As of the data cut-off, the most common treatment related AEs included skin and subcutaneous tissue disorders (97%), gastrointestinal disorders (77.8%), and infections and infestations (74.7%).[4]

"This FDA filing acceptance marks a significant milestone for Ipsen and those living with this relentless condition of FOP, which we hope will have a significant impact," said Robert J. Pignolo, M.D., Ph.D., Chair, Geriatric Medicine & Gerontology, Mayo Clinic College of Medicine. "News of this potential new treatment will be welcomed by the FOP community, and we await further updates from the FDA. With ultra-rare conditions by their nature

affecting very few people around the world it is so important we continue to make progress and advance the management of diseases like FOP."

In addition to the European Medicines Agency (EMA) and Swissmedic MAA validations, Ipsen anticipates additional applications to other regulatory agencies in due course.

ENDS

About the palovarotene FOP clinical program

The Phase III MOVE (NCT03312634) trial is an ongoing open-label, single-arm trial evaluating the efficacy and safety of a chronic/flare-up dosing regimen of palovarotene, which comprises a 5mg daily dose that is increased at the start of a flare-up to 20mg for four weeks, followed by 10mg for eight weeks. At the end of the flare-up dosing period, the dose returns to the chronic 5mg daily dose. All dosing is weight-adjusted in skeletally immature participants (those under the age of 18 years with less than 90% skeletal maturity on hand/wrist x-rays performed at screening). 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, multi-center 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 participants under the age of 14 years participating in the Phase II (PVO-1A-202/204 and PVO-2A-201) and Phase III (PVO-1A-301) studies at all clinical sites globally. This was due to reports of premature physeal closure (PPC). A decision to pause dosing of palovarotene in all remaining 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 January 24, 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 as of March 26, 2020 across the Phase II and Phase III programs for palovarotene in FOP.

About palovarotene

Palovarotene is an oral investigational, selective retinoic-acid receptor gamma (RARγ) agonist being developed as a potential treatment for people living with the debilitating ultra-rare genetic disorder fibrodysplasia ossificans progressiva (FOP). Palovarotene, which received rare pediatric disease and breakthrough therapy designations from the FDA for the potential 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.[3] FOP has an estimated prevalence of 1.36 per million individuals; however, the number of confirmed cases varies by country.[1,2]

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 2020, 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).

Contacts

Investors

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

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

Media

Jess Smith
Senior Director, Global Communications, R&D and Business Development
+44 7557 267 634

Maryann Quinn
Director, Product Communications North America
+1 857 529 1151

References

[1] Lilijesthrom, M & Bogard, B 2016, 'The global known FOP population', FOP Drug Development Forum, Boston, MA, 24-25 October.

[2] Baujat et al. Prevalence of fibrodysplasia ossificans progressiva (FOP) in France: an estimate based on a record linkage of two national databases. Orphanet Journal of Rare Diseases. 2017; 12:123.

[3] Kaplan FS, et al. The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. Proc Intl Clin Council FOP 1:1-111, 2019.

[4] Pignolo R, Al Mukaddam, M, Baujat, G, Berglund, S, Cheung, A, De Cunto, C, Delai, P, Di Rocco, M, Haga, N, Hsiao, E, Kannu, P, Keen, R, Mancilla, E, Grogan, D, Marino, R, Strahs, A & Kaplan, F 2020, 'Palovarotene (PVO) for fibrodysplasia ossificans progressiva (FOP): data from the phase III MOVE trial', ASBMR Virtual Meeting, 11-15 September.

[5] ClinicalTrials.gov. An efficacy and safety study of palovarotene for the treatment of fibrodysplasia ossificans progressiva. (MOVE), clinicaltrials.gov, viewed March 2021, <https://clinicaltrials.gov/ct2/show/NCT03312634>.
©2021 Ipsen Biopharmaceuticals, Inc. May 2021 NON-US-002389