PRESS RELEASE

Ipsen to present new data on clinical outcomes and patient validation tools from growing rare liver disease portfolio at EASL 2023

- Seven abstracts to be presented demonstrating treatment effects of Bylvay® in two cholestatic liver diseases, progressive familial intrahepatic cholestasis and Alagille syndrome
- Data to be presented from a qualitative trial on patient validation of pruritus (itch) and fatigue assessment tools for people living with primary biliary cholangitis (PBC), used as part of the ELATIVE Phase III registrational trial for elafibranor

PARIS, FRANCE, 12 June 2023 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the company will present data from across its growing rare liver disease portfolio, at the European Association for the Trial of Liver (EASL) Congress 2023, 21-24 June in Vienna, Austria. These include seven abstracts on new clinical data being presented on Bylvay® (odevixibat) when used in patients with progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome (ALGS). In addition, an abstract on content validation of patient-reported outcomes assessment tools, used with patients with primary biliary cholangitis (PBC), is being presented.

The Bylvay abstracts provide further understanding of the treatment's efficacy and safety profile, when used in sub-groups of both paediatric and adult patients with PFIC. The data report on outcomes including event free survival, reduction in serum bile acids (sBAs), pruritus and other quality of life outcomes, in long-term clinical trial and real-world settings. In the investigational Bylvay indication for patients with ALGS, new pooled data from the Phase III ASSERT trial and extension studies demonstrate significant improvements in pruritus and sBAs and sleep disturbances.

The patient-reported outcomes assessment tools, include the PBC Worst Itch Numeric Rating Scale (PBC WI NRS) and PROMIS Fatigue Short Form 7a (PFSF 7a), are being used to assess symptoms in ELATIVE, a Phase III clinical trial of elafibranor, an investigational therapy for PBC. The tools have been designed to derive meaningful change thresholds among patients with PBC experiencing symptoms like pruritus (itch) and fatigue. PBC is a disease where symptoms can be debilitating for patients and have a significant impact on their quality of life.[1, 2]

Finally, two abstracts will be presented on pre-clinical data from two pipeline assets under investigation for further cholestatic diseases.

"We look forward to presenting additional data from our Phase III Bylvay trials in both PFIC and ALGS, in addition to data supporting the validation of the patient report outcome tools we are using in our Phase III trial ELATIVE, with investigational elafibranor, amongst the scientific peer group attending EASL 2023," said Dr. Howard Mayer, Executive Vice President and Head of Research and Development, Ipsen. "These data highlight our ongoing focus on supporting the communities of patients living with rare liver disease by better understanding their needs and furthering research on potential treatment options."

Highlights from key data to be presented during the EASL congress 2023 include:

- Analysis of long-term treatment effects of Bylvay in children with PFIC compared to matched, non-Bylvay treated patients from the NAtural Course and Prognosis of PFIC and Effect of Biliary Diversion (NAPPED) registry.
- Outcomes from a case trial focused on the treatment of Bylvay in patients with PFIC with the MYO5B mutation.
- Discoveries from a subgroup in the PEDFIC 2 trial, showing Bylvay's efficacy and tolerability in adults with PFIC.

- A real-world case series demonstrating Bylvay's effectiveness and safety in adults with genetic cholestasis disorders.
- Pooled data from ASSERT Phase III and ASSERT-EXT studies, showing efficacy and safety outcomes after 36-weeks of treatment.
- Insights from AS03969 and A3907, early stage ASBT inhibitors, in development for adult liver diseases.
- Trial results on the relevance and importance of the Primary Biliary Cholangitis Worst Itch Numerical Rating Scale (PBC WI NRS) and PROMIS Fatigue Short Form 7a (PFSF 7a), two clinical outcome assessment tools for symptomatic patients living with PBC.

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Full presentation details:

Poster (Abstract #1511): Analysis of long-term treatment effects of odevixibat on clinical outcomes in children with progressive familial intrahepatic cholestasis in odevixibat clinical studies vs external controls from the NAPPED database.
Presenter: Bettina Hansen, Department of Epidemiology & Biostatistics, Erasmus MC, Rotterdam, the Netherlands; Toronto Centre for Liver Disease & TGHRI, University Health Network, Canada; IHPME, University of Toronto, Toronto, Canada
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #912): Efficacy and safety outcomes with odevixibat treatment: Pooled data from the Phase 3 ASSERT and ASSERT-EXT studies in patients with Alagille syndrome
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #1031): Outcomes in adult patients with progressive familial intrahepatic cholestasis treated with odevixibat: subgroup analysis from the PEDFIC 2 trial
Presenter: Henkjan Verkade, Department of Paediatrics, University of Groningen, Beatrix Children's Hospital/University Medical Centre Groningen, Groningen, the Netherlands
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #1039): Real-world experience of odevixibat in adults with genetic disorders of cholestasis
Presenter: Palak Trivedi, National Institute for Health Research Birmingham Biomedical Research Centre, Centre for Liver and Gastrointestinal Research, University of Birmingham, Birmingham, UK
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #1013): Long-term efficacy and safety of odevixibat in patients with progressive familial intrahepatic cholestasis: results with 96 weeks or more of treatment
Presenter: Ekkehard Sturm, Paediatric Gastroenterology and Hepatology, University Children's Hospital Tübingen, Tübingen, Germany
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #1017): Odevixibat therapy following liver transplantation in patients with FIC1-deficient progressive familial intrahepatic cholestasis: a retrospective case series
Presenter: Georg-Friedrich Vogel, Department of Paediatrics I, Medical University of Innsbruck, Innsbruck, Austria; Institute of Cell Biology, Medical University of Innsbruck, Innsbruck, Austria
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract #1323): Odevixibat therapy in patients with MYO5B mutations: a retrospective case series
Presenter: Emmanuel Gonzalès, Hépatologie et Transplantation Hépatique Pédiatriques, Hôpital Bicêtre, Paris, France
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Poster (Abstract 1067): Evaluating pruritus and fatigue in patients with treatment-refractory primary biliary cholangitis
Presenters: Peter Serafini, Director Global Market Access and Marwan Sleiman, Global Medical Affairs Director, Ipsen
Session title: Rare liver diseases (including paediatric and genetic)
Date and time: 22nd June, 09:00-18:00 CEST

Poster (Abstract #1325): Inhibition of the renal apical sodium-dependent bile acid transporter prevents cholemic nephropathy
Presenter: Ahmed Ghallab, Department of Toxicology, Leibniz Research Centre for Working Environment and Human Factors, Technical University Dortmund, Ardeystr 67, 44139, Dortmund, Germany
Session title: Poster - Rare liver diseases
Date and time: June 22, 2023 | 9:00-18:30

Oral (ID OS-074-YI): A3907, a systemic ASBT inhibitor, improves cholestasis in mice by inhibiting multi-organ bile acid transport and shows translational relevance to humans
Presenter: Francisco J. Caballero-Camino, Department of Liver and Gastrointestinal Diseases, Biodonostia Health Research Institute – Donostia University Hospital, University of the Basque Country (UPV/EHU), San Sebastian, Spain
Session title: Immune-mediated and cholestatic diseases
Date and time: June 24, 2023 | 15-15:15

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About the Phase III PEDFIC studies
The PEDFIC trials represent the largest studies ever completed in children with PFIC, or progressive familial intrahepatic cholestasis, a rare genetic disorder that causes progressive, life-threatening liver disease. PEDFIC 1 was a randomized, double-blind, placebo-controlled Phase III trial that evaluated the efficacy and tolerability of Bylvay in reducing pruritus and serum bile acids (sBAs) in children with PFIC, and PEDFIC 2 is a long-term, open-label Phase III extension trial. Patients with PFIC have impaired bile flow, or cholestasis, and the resulting bile build-up in liver cells causes liver disease and symptoms, such as intense itching, poor sleep, delayed growth, and diminished quality of life. The harmful impacts of the disease extend to parents and caregivers, as the 2022 multinational PICTURE trial revealed that PFIC negatively affects caregivers' quality of life, relationships, and career prospects.

About the Phase III ASSERT trial
ASSERT is a gold standard, prospective intervention trial with 32 sites across North America, Europe, Middle East, and Asia Pacific. The double-blind, randomized, placebo-controlled trial was designed to evaluate the safety and efficacy of 120 µg /kg/day Bylvay for 24 weeks in relieving pruritus in patients with ALGS. Key secondary endpoints measure serum bile acid levels and safety and tolerability. The trial enrolled patients aged 0 to 17 years of age with a genetically confirmed diagnosis of ALGS. In the primary analysis, the trial met the primary endpoint showing statistically significant reduction in pruritus as measured by the PRUCISION Observer-Reported Outcome scratching score (0-4 point scale), from baseline at month 6 (weeks 21 to 24), compared to the placebo arm (p=0.002). Over 90% of patients were pruritus responders during the trial, as defined as at least a 1-point drop at any time point. The trial also met the key secondary endpoint showing a statistically significant reduction in serum bile acid concentration from

baseline to the average of weeks 20 and 24 (compared to the placebo arm p=0.001). Statistically significant improvements in multiple sleep parameters were observed as early as week 1-4 compared to patients on placebo with continued improvement through week 24. In the trial, there were no patient discontinuations. Bylvay was well tolerated, with an overall adverse event incidence similar to placebo and a low incidence of drug-related diarrhea (11.4% vs. 5.9% placebo).

About Bylvay® (odevixibat)
Bylvay is a potent, once-daily, non-systemic IBATi that acts locally in the small intestine and has minimal systemic exposure. It is approved in the U.S. for the treatment of pruritus in patients three months of age and older with PFIC, where it has orphan exclusivity. Bylvay was first launched as a treatment option for patients with PFIC in the U.S. in 2021, where it is supported by a program designed to assist with access to treatment and patient support. Bylvay is also approved in the E.U. for the treatment of PFIC in patients aged six months or older. It has launched in over nine countries and has secured public reimbursement across several major markets including Germany, Italy, the U.K., France and Belgium.

View full E.U. prescribing information here: **Bylvay, INN-odevixibat (europa.eu)**
View full U.S. prescribing information here: **label (fda.gov)**

About the PBC trial: Evaluating pruritus and fatigue in patients with treatment-refractory primary biliary cholangitis
Semi-structured qualitative interviews were conducted with 20 patients (aged 28-68 years; 19 females) diagnosed with PBC, (mean 10.7 years since diagnosis) experiencing pruritus (mild [30%], moderate [45%] or severe [25%]), using Institutional Review Board-approved materials. The PFSF 7a consists of 7 items that measure both the experience of fatigue and interference of fatigue on daily activities over the past 7 days using a Likert response scale. Patients were asked to evaluate the PBC WI NRS and PFSF 7a on ease of understanding of instructions and items, ease of use of scale/response options, and appropriateness of recall period to capture the patient experience. Interviews were conducted by experienced qualitative researchers, and audio recordings were transcribed and analyzed with coding software.

About Elafibranor
Elafibranor is a novel, oral, once-daily, dual peroxisome activated receptor (PPAR) alpha/delta (α,δ) agonist, currently under investigation as treatment for patients with PBC, a rare liver disease. In 2019, it was granted a Breakthrough Therapy designation by the FDA in adults with PBC who have an inadequate response to ursodeoxycholic acid (UDCA). Elafibranor has not received approval by regulatory authorities anywhere in the world.

About Ipsen
Ipsen is a global, mid-sized biopharmaceutical company focused on transformative medicines in Oncology, Rare Disease and Neuroscience. With total sales of €3.0bn in FY 2022, 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 5,400 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

References:
1. Mells GF et al. Hepatology. 2013 ; 58 : 273-283
2. Poupon RE et al. Hepatology. 2004 ; 40(2) : 489-494

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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

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