Press Release

Ojemda® approved in the European Union as the first targeted therapy in relapsed or refractory pediatric low-grade glioma regardless of BRAF alteration

- New treatment option for rare, life-altering pediatric brain tumors
- Less than 10% of new medicine approvals over the past five years have focused on pediatric diseases; Ojemda® (tovorafenib) represents a rare achievement that reinforces the urgent need to close the innovation and investment gaps in pediatric therapeutics
- Approval is based on pivotal Phase II FIREFLY-1 data[i] demonstrating meaningful and durable tumor responses

PARIS, FRANCE, 22 April 2026 — Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the European Commission (EC) has granted conditional marketing authorization for Ojemda® (tovorafenib) as monotherapy for the treatment of patients 6 months of age and older with pediatric low-grade-glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation, who have progressed after one or more prior systemic therapies.[ii] This EC decision applies across all 27 EU Member States, as well as Iceland, Liechtenstein, and Norway.

More than 800 children are diagnosed with BRAF altered pediatric low-grade glioma (pLGG) each year in the EU.[iii] This brain tumor, while classified as low-grade (slow progression) carries a profound lifelong burden, frequently leading to significant physical and neurological impairments including loss of vision, speech difficulties and motor dysfunction, which can significantly impact a child's education, independence and long-term quality of life.[iv]

Until now, many children living with pLGG have had to go through invasive surgeries, multiple lines of chemotherapy, and radiotherapy, often resulting in health complications.[v]

"For children diagnosed with low-grade glioma, the journey is often long and challenging with limited available treatment options," said Sandra Silvestri, M.D., PhD, Executive Vice President and Chief Medical Officer, Ipsen. "Today's approval is a meaningful step forward for these children, and their families, while reinforcing our commitment to addressing high unmet need. Now, our focus is on ensuring that eligible children across Europe can access this therapy as quickly as possible."

The EC approval is based on data from the pivotal Phase II FIREFLY-1 study[i] which evaluated tovorafenib in 137 children and young adults with relapsed or refractory BRAF-altered pLGG who had received at least one prior systemic therapy. The study demonstrated:

- **Clinically meaningful tumor response:** An overall response rate of 71% per the Response Assessment in Neuro-Oncology criteria for High-Grade Gliomas (RANO-HGG) criteria and 53% per Response Assessment in Pediatric Neuro-Oncology for Low-Grade Glioma (RAPNO-LGG) criteria, with a clinical benefit rate of 77% per RANO-HGG criteria and 58% per RAPNO-LGG criteria.[vi]
- **Rapid and durable responses**: Based on RAPNO-LGG criteria, among responders, the median time to response was 5.4 months with a median duration of response of 18.0 months.[vii]
- **Manageable safety profile:** Tovorafenib was generally well-tolerated, with predominantly Grade 1 or 2 treatment-related adverse events (TRAEs) and a low discontinuation rate (9.5% patients discontinued treatment due to events considered by the investigator to be related to tovorafenib).[vii] The most common TRAEs were hair color changes, blood creatine phosphokinase increased, fatigue, anemia, vomiting, hypophosphataemia, headache, rash maculo-papular, pyrexia, growth retardation, dry skin.[vii]
- **Convenient Dosing:** Once-weekly oral administration, with or without food, in liquid or tablet formulation, minimizing disruption to daily family routine.[ii]

"Families affected by low-grade glioma often endure years of uncertainty, difficult treatment decisions, and the fear of long-term consequences," said Professor François Doz, Professor of Pediatrics at Paris Descartes University, Deputy Director of Clinical Research, Innovation and Teaching in the SIREDO Oncology Centre of the Curie Institute (Care, Innovation and research in Cancer of the child, adolescent and young adult) and Director of Teaching of the Hospital Ensemble of the Institut Curie. "The approval of a targeted therapy like tovorafenib represents a major step forward, offering families not only a new treatment option, but a renewed optimism."

The EU Health Technology Assessment (HTA) Regulation, which began phasing in from January 2025, introduced a new Joint Clinical Assessment (JCA) process to streamline and harmonize the comparative clinical evidence review across EU Member States. Ojemda is the first medicine to undergo a JCA evaluation.

About tovorafenib

Tovorafenib (known as Ojemda®) is a Type II RAF kinase inhibitor of mutant BRAF V600, wild-type BRAF, and wild-type CRAF kinases. It targets the signaling pathways regulating cell growth and division, which can slow, stop, or shrink cancerous tumors.

Tovorafenib is indicated for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation.[vii]

It was approved by the U.S. FDA under accelerated approval[viii] based, in part, on response rate and duration of response according to multiple response assessment criteria: Response Assessment in Neuro-Oncology High-Grade Glioma (RANO-HGG) criteria, Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma (RAPNO-LGG) criteria, and Response Assessment for Neuro-Oncology Low-Grade Glioma (RANO-LGG) criteria. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Tovorafenib is under evaluation as a therapy for patients aged less than 25 years with pLGG harboring BRAF fusion or rearrangement, or BRAF V600 mutation requiring front-line treatment (Phase III FIREFLY-

2/LOGGIC). Additional information about FIREFLY-2 may be found at ClinicalTrials.gov, using Identifier NCT05566795 and at CTIS under EUCT number 2024-510742-13-00.

The medicine was granted Breakthrough Therapy and Rare Pediatric Disease designations by the FDA for the treatment of patients with pLGG harboring an activating RAF alteration, and it was evaluated by the FDA under priority review. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma and from the European Commission for the treatment of glioma. Tovorafenib has also been approved in EAU and has been granted Orphan Drug Designation in Russia, Switzerland, Taiwan, Japan South Korea and Australia.

Ipsen licensed the ex-U.S. rights to tovorafenib from Day One Biopharmaceuticals Inc in 2024.

About FIREFLY-1[i]

FIREFLY-1 is evaluating tovorafenib as once-weekly monotherapy in patients aged 6 months to 25 years with relapsed or progressive pLGG harboring a known activating BRAF alteration.

The trial is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium. The pivotal and ongoing Phase II FIREFLY-1 study evaluated the safety and efficacy of tovorafenib in 137 relapsed or refractory BRAF-altered pLGG patients, who had received at least one line of prior therapy, across two study arms. Arm 1 (n=77) was used for the efficacy analyses and Arm 2 provided safety data for an additional 60 patients, initiated to enable access to tovorafenib once Arm 1 had fully recruited.

Additional information about FIREFLY-1 may be found at ClinicalTrials.gov, using Identifier NCT04775485 and at CTIS under EUCT number 2024-510691-20-00.

About pediatric low-grade glioma

Pediatric low-grade glioma (pLGG) is a rare childhood brain tumor. More than 800 new cases of BRAF altered pLGG are identified in the European Union each year.[iii,] BRAF is the gene most commonly altered in pLGG, which include two primary types of BRAF alterations – a BRAF gene fusion and BRAF V600E mutation.[ix] These BRAF alterations account for more than 50% of pLGG cases worldwide and until recently there were no approved treatments for patients with pLGG driven by BRAF fusions.[x]

pLGG can be chronic and relentless, with patients suffering profound side effects from both the tumor and the treatment, which may include chemotherapy and radiation.[iv] These side effects can impact their life over the long term, and may include muscle weakness, loss of vision, and difficulty speaking. This type of tumor has a high risk of progression, and many children with pLGG require long-term treatment.[v] While most children with pLGG survive their cancer, children who do not achieve a complete resection following surgery may face years of increasingly aggressive treatment.

About Ipsen

We are a global biopharmaceutical company with a focus on bringing transformative medicines to patients in three therapeutic areas: Oncology, Rare Disease and Neuroscience. Our pipeline is fueled by internal and external innovation and supported by nearly 100 years of development experience and global hubs in the U.S., France and the U.K. Our teams in more than 40 countries and our partnerships around the world enable us to bring medicines to patients in more than 100 countries.

Ipsen 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.

Ipsen Contacts

Investors

Henry Wheeler	henry.wheeler@ipsen.com	+33 7 66 47 11 49
Khalid Deojee	khalid.deojee@ipsen.com	+33 6 66 01 95 26

Media

Sally Bain	sally.bain@ipsen.com	+1 857 320 0517
Anne Liontas	anne.liontas.ext@ipsen.com	+33 7 67 34 72 96

Disclaimers and/or 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 and risks arising from unexpected regulatory or political changes such as changes in tax regulation and regulations on trade and tariffs, such as protectionist measures, especially in the United States; 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 latest Universal Registration Document, available on ipsen.com.

References:

[i] Kilburn LB, *et al.* The type II RAF inhibitor tovorafenib in relapsed/refractory pediatric low-grade glioma: the phase 2 FIREFLY-1 trial. *Nat Med*. 2024;30(1):207–217.
[ii] European Medicines Agency (EMA) Ojemda® (tovorafenib) Summary of Product Characteristics (SmPC)
[iii] Estimates of annual incidence and prevalence for addressable patient population in E.U. 4 + U.K. are based on Ipsen calculations from publicly available data (Eurostat, <25yo population; Global Burden of Disease 2019; Desandes et al. Incidence and survival of children with central nervous system primitive tumors in the French National Registry of Childhood Solid Tumors. Neuro Oncol. 2014 Jul;16(7):975-83. doi: 10.1093/neuonc/not309; Qaddoumi et al. Outcome and prognostic features in pediatric gliomas: a review of 6212 cases from the Surveillance, Epidemiology, and End Results database. Cancer. 2009 Dec 15;115(24):5761-70. doi: 10.1002/cncr.24663)
[iv] Dana-Farber Cancer Institute. Childhood Low-Grade Gliomas. Available at: https://www.dana-farber.org/cancer-care/types/childhood-low-grade-gliomas. Accessed March 2026
[v] Pediatric Brain Tumor Foundation. Voice of the Patient Report. August 5, 2024. Accessed March 2026.
[vi] Data on file, data from FIREFLY-1 study, data cut off 10 May 2024, submitted to EMA
[vii] Tovorafenib US prescribing information 2024
[viii] Day One Press Release. April 2024. Available here: Day One's OJEMDA™ (tovorafenib) Receives US FDA Accelerated Approval for Relapsed | Day One Biopharmaceuticals, Inc. Accessed March 2026.
[ix] Ryall S, et al. *Acta Neuropathol Commun*. 2020;8(1):30.
[x] Ryall S, et al. Integrated molecular and clinical analysis of 1,000 pediatric low-grade gliomas. Cancer Cell. 2020;37(4):569–583.e5.