Press Release

Ipsen receives positive CHMP opinion for Ojemda® for the treatment as monotherapy of children with relapsed or refractory BRAF-altered pediatric low-grade glioma

- If approved, Ojemda® (tovorafenib) is expected to be the first and only targeted medicine in European Union for children with relapsed or refractory BRAF-altered pediatric low-grade glioma, irrespective of the type of BRAF alteration[i]
- The decision is based on data from the pivotal Phase II FIREFLY-1 study which demonstrated clinically meaningful and durable tumor responses with a positive impact on children's lives[ii]

PARIS, FRANCE, 27 FEBRUARY 2026 – Ipsen (Euronext: IPN; ADR: IPSEY) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending the conditional marketing authorization of Ojemda® (tovorafenib) as monotherapy for the treatment of patients 6 months of age and older with paediatric low-grade glioma (pLGG) harbouring a BRAF fusion or rearrangement or BRAF V600 mutation, who have progressed after one or more prior systemic therapies.[i]

More than 800 new cases of BRAF altered pLGG are identified in the European Union each year,[iii] causing multiple disabilities including sight, speech, and other neurological problems that profoundly impact the lives of children and their families.[iv] The treatment journey for these patients is also complex, often involving invasive surgeries, multiple lines of intensive chemotherapy and radiotherapy over many years, leading to lifelong health issues and developmental complications.[v]

"For children diagnosed with pediatric low-grade glioma, the journey is long and complex, with limited treatment options and no clear standard of care," said Christelle Huguet, PhD, EVP and Head of Research & Development, Ipsen. "Innovating in pediatric oncology is challenging, and genuine breakthroughs are rare. The evidence supporting tovorafenib, which acts on tumor growth driven by an abnormal BRAF gene, is an important development. The positive CHMP opinion moves us closer to delivering a meaningful targeted therapy for these patients and their families."

Today, there is no global uniform consensus on standard of care for most children as they progress with this rare brain tumor,[vi] and there is a considerable need for approved therapies that can minimize long-term morbidities and maintain or improve overall quality of life.

"Treatment options for relapsed/refractory pediatric low-grade glioma have remained limited for decades, which is why a targeted therapy like tovorafenib has the potential to transform how we manage this disease in particular the most common subtype carrying the BRAF-Fusion oncogene," said

Professor Olaf Witt, Director, Translational Pediatric Oncology, Hopp Children's Cancer Center Heidelberg. "As a treating physician, I am encouraged by the prospect of introducing a new treatment option for this challenging condition in Europe."

The CHMP's positive opinion is based on data from the pivotal Phase II FIREFLY-1 study,[ii] 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 Paediatric 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.[vii]

- **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] Common TRAEs included hair color changes, elevated creatine phosphokinase, fatigue and anemia.[vii]

- **Convenient Dosing:** Once-weekly oral administration, with or without food, in liquid or tablet formulation, minimizing disruption to daily family routine.[i]

Following this positive opinion, the European Commission will review the CHMP's recommendation, with a final decision on marketing authorization expected in the coming months.

About tovorafenib

Tovorafenib (known as OJEMDA™ in the U.S.) 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.

In the U.S, tovorafenib is indicated for the treatment of people 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation.[viii] It was approved by the U.S. FDA under accelerated approval[ix] 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).

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 granted Orphan Drug Designation in South Korea.

Ipsen licensed the rights to tovorafenib from Day One Biopharmaceuticals Inc in 2024.

About FIREFLY-1[ii]

FIREFLY-1 is evaluating tovorafenib as once-weekly monotherapy in people 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.[x] These BRAF alterations account for more than 50% of pLGG cases worldwide and until recently there were no approved treatments for people with pLGG driven by BRAF fusions.[vi]

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.

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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:

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[vii] Data on file, data from FIREFLY-1 study, data cut off 10 May 2024, submitted to EMA
[viii] Tovorafenib US prescribing information 2024
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[x] Ryall S, et al. *Acta Neuropathol Commun*. 2020;8(1):30.