Orphelia Pharma provides update on the regulatory submission of KIZFIZO® with the European Medicines Agency

Orphelia to seek re-examination following CHMP negative opinion for the treatment of relapsed or refractory high-risk neuroblastoma

Paris and Lyon, France, November 18, 2024 – Orphelia Pharma, a pharmaceutical company dedicated to the development and marketing of pediatric and orphan medicines, announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a negative opinion on the Marketing Authorization Application for KIZFIZO (temozolomide oral suspension) for the treatment of patients with relapsed or refractory high-risk neuroblastoma, because the CHMP considered that a positive benefit-risk balance has not been established at this stage. Orphelia will seek a re-examination of the opinion by the CHMP.

"We are extremely disappointed by the CHMP's negative opinion and understand that this may also be disappointing for the pediatric oncology community as well as for parents of children suffering from cancer." said Jérémy Bastid, Chief Medical Officer at Orphelia Pharma. "There is a significant demand for developing children-adapted formulations. Orphelia Pharma has been developing KIZFIZO in collaboration with Gustave Roussy, the leading European cancer center, for the last seven years specifically to address this unmet medical need for a drinkable temozolomide medication in the treatment of relapsed or refractory neuroblastoma, which affects very young children".

"As part of the re-examination process, we will seek to address the CHMP's grounds for refusal and we will work diligently to substantiate the clinical benefit of the treatment so that KIZFIZO can be available to pediatric patients in the EU without further delay" commented Laurent Martin, Chief Pharmaceutical Affairs Officer at Orphelia Pharma.

In the meantime, Orphelia Pharma will, subject to agreement by the relevant authorities, continue to make KIZFIZO available to pediatric patients suffering from relapsed or refractory neuroblastoma under compassionate use or early access programs as well as to patients enrolled into ongoing clinical trials.

About KIZFIZO® 40 mg/ml

KIZFIZO (temozolomide oral suspension, 40 mg/ml) is a ready-to-use oral liquid pediatric formulation of temozolomide developed/designed specifically for use in the treatment of children with relapsed or refractory high-risk neuroblastoma, which carries a very poor prognosis. This age-adapted and taste-masked formulation delivers an accurate dose in a small volume, while avoiding drug handling and caregiver exposure to temozolomide. It is the result of a collaboration between the pharmacists and clinicians at Gustave Roussy hospital and the development team at Orphelia Pharma.

In March 2022, KIZFIZO was granted Early Access Authorization (Autorisation d'Accès Précoce) by the French authorities, for the treatment of refractory and relapsed neuroblastoma as monotherapy or in combination with irinotecan or topotecan.

KIZFIZO has received Orphan Drug Designation (ODD) from the EMA and the FDA, the formulation is covered by granted patents and pending applications in Europe and the US.

The pharmacokinetics of KIZFIZO in children have been evaluated in *TEMOkids*, a European multicenter population pharmacokinetic acceptability and safety study in pediatric patients in need of temozolomide (NCT04610736).

Efficacy and safety data for temozolomide in relapsed or refractory neuroblastoma submitted in the application includes in particular:

- *BEACON-Chemo*, a sub-analysis of the chemotherapy arms of the *BEACON* study, a prospective randomized phase II study in refractory or relapsed neuroblastoma. This study was sponsored by Birmingham University (UK).
- *Retro-TMZ*, a multicenter descriptive, retrospective study, assessing the efficacy and tolerability of temozolomide in children with refractory or relapsed neuroblastoma. This study was conducted by Gustave Roussy (France).

About Neuroblastoma

Neuroblastoma is the most common extracranial cancer in early childhood, with approximately 900 new cases diagnosed per year in the European Union. It almost exclusively affects children under five, with a median age at diagnosis of 18 months. Neuroblastoma has a wide diversity of clinical outcomes, which is reflected in the risk stratification. Approximately 40% of patients have the high-risk disease and often face a poor response to first line induction therapy or later relapse. There remains a high unmet need for relapsed or refractory neuroblastoma patients and the best therapeutic strategy is still an intensive area of research. Temozolomide is the standard chemotherapy and is therefore an essential part of the treatment armamentarium for these patients.

About Orphelia Pharma

Orphelia Pharma is a pharmaceutical company based in Paris and Lyon that develops and markets medicines for the treatment of pediatric and orphan diseases. The company's mission is to provide patients with essential products in the fields of neurology and oncology, in formulations adapted to the pediatric population. Orphelia Pharma conducts research projects through academic and industrial partnerships. It has recently established regional agreements in European territories and is expanding its footprint across the world.

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