ONO PHARMA USA, INC.

March 22, 2023

ONO PHARMA USA's Tirabrutinib Receives Orphan Drug Designation from the FDA for the Treatment of Primary Central Nervous System Lymphoma

CAMBRIDGE, Mass. -- ONO PHARMA USA, INC., announced that its candidate, tirabrutinib (ONO-4059), a Bruton's tyrosine kinase inhibitor, was granted Orphan Drug Designation on March 21, 2023 by the U.S. Food and Drug Administration (FDA) for the treatment of patients with primary central nervous system lymphoma (PCNSL).

The FDA's Orphan Drug Designation program supports the development and evaluation of investigational drugs and biologics that show promise for the diagnosis, treatment, or prevention of rare diseases or disorders, affecting fewer than 200,000 people in the United States (U.S.).

PCNSL is a rare and aggressive extra nodal non-Hodgkin lymphoma affecting the brain, its protective membranes, the spinal cord, and/or eye, without systemic involvement at the time of diagnosis. In the U.S., the incidence of PCNSL is approximately five out of 1,000,000 people per year, with higher rates in people over 65 years old.[1] Symptoms can vary depending on the location of the tumor and may include headache, nausea, vomiting, visual symptoms, and seizures, among others. ONO is currently recruiting newly diagnosed and relapsed or refractory adult PCNSL patients in the U.S. for the PROSPECT clinical study (www.theprospectstudy.com; NCT04947319).

"We are extremely pleased that tirabrutinib has been granted orphan drug status for the treatment of PCNSL," said Kunihiko Ito, President and CEO of ONO PHARMA USA. "The designation represents a milestone for ONO. Currently, ONO is carrying out a Phase 2 trial of tirabrutinib in people with newly diagnosed or relapsed/refractory PCNSL, and we look forward to advancing clinical trials so that patients may have therapeutic options as soon as possible."

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About PCNSL

PCNSL is a rare and aggressive extra nodal non-Hodgkin lymphoma (NHL) that is confined to the brain parenchyma, spinal cord, eye, or leptomeninges, without systemic involvement. The annual incidence rate of PCNSL is approximately five cases per 1,000,000 people in the U.S. The rate can further increase among immunocompetent people aged 65 years and older. The signs and symptoms presented in patients with PCNSL vary depending on the neuroanatomical site of the lesion, and include cranial neuropathy, neuropsychiatric symptoms, symptoms associated with increased intracranial pressure, seizures, ocular symptoms, headache, dysmotility, cranial neuropathy, and radiculopathy. There are no therapeutic products specifically approved for the treatment of PCNSL in the U.S., and data guiding therapeutic approaches are very limited. Despite recent progress resulting in the improvement of clinical outcomes in newly diagnosed patients with PCNSL after an induction treatment, approximately 20 to 30 percent of patients are refractory to the initial treatment, and up to 60 percent of patients will eventually relapse.

About Tirabrutinib

Tirabrutinib, discovered and developed by Ono Pharmaceutical Co., Ltd., is a highly potent selective BTK inhibitor. Signaling through the B-cell receptor (BCR) regulates cellular proliferation and activation, and promotes survival, differentiation, and clonal expansion of B-cells. The BCR signaling pathway plays an important role in a number of B-cell malignancies. Gene expression profiling data revealed BCR signaling as the most prominent pathway activated in chronic lymphocytic leukemia (CLL) cells isolated from lymphatic tissues. In Japan, tirabrutinib was approved in March 2020 for the treatment of relapsed or refractory PCNSL and launched under the tradename of Velexbru® in May 2020. In addition, tirabrutinib was approved for the treatment of relapsed or refractory PCNSL in South Korea in November 2021 and in Taiwan in February 2022. Moreover, Velexbru® was approved for the treatment of Waldenstrom macroglobulinemia and lymphoplasmacytic lymphoma in Japan in August 2020.

About the PROSPECT Study

The PROSPECT Study is the Phase 2 trial (NCT04947319) evaluating the safety and effectiveness of an investigational oral medicine called tirabrutinib for potential treatment of newly diagnosed or relapsed/refractory primary central nervous system lymphoma, which is a type of cancer that either does not improve from treatment (refractory) or improves only for a limited time (relapsed). Current treatment options for relapsed or refractory PCNSL are limited, and there are no medications approved in the U.S. for the treatment of PCNSL. Learn more about the PROSPECT Study here: www.theprospectstudy.com.

About ONO PHARMA USA

ONO PHARMA USA is the U.S. subsidiary of Ono Pharmaceutical Co., Ltd. ("ONO"), a Japanese pharmaceutical company. For more than 300 years, ONO has been focused on developing safe, high-quality, and effective therapies that help people lead healthier lives. ONO is dedicated to pursuing the clinical development of new therapeutic candidates for the U.S. market. ONO is also engaged in strategic alliances, partnerships, and licensing activities to expand its development and commercialization pipeline. For more information, please visit www.ono-usa.com.

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Reference

1. Ostrom QT, Price M, Neff C, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015-2019. *Neuro Oncol*. 2022;24(Suppl 5): v1-v95.