ONO PHARMA

Press Release

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Ono Pharmaceutical Co., Ltd.

# ONO PHARMA Announces Enrollment is Complete for the First Arm of the PROSPECT Study of Tirabrutinib in U.S. Patients with Relapsed or Refractory PCNSL

*Primary central nervous system lymphoma (PCNSL) is a rare and aggressive lymphoma with no approved treatment in the U.S.*[1]

OSAKA, JAPAN, March 21, 2024 /PRNewswire/ -- ONO Pharmaceuticals, Co., Ltd. today announced it has completed target patient enrollment of the first arm (Part A) of the PROSPECT Study, a Phase 2 clinical trial evaluating the safety and efficacy of tirabrutinib (ONO-4059) in U.S. patients with relapsed or refractory primary central nervous system lymphoma (R/R PCNSL).

“A PCNSL diagnosis can be frightening for patients, and treatment options approved by the FDA are critically needed in the U.S.,” said Kiyoaki Idemitsu, Executive Officer / Executive Director, Clinical Development of ONO PHARMA. “Completing enrollment of the first arm of this U.S. study is an important step in bringing a therapeutic option to patients with R/R PCNSL in the U.S. We are very grateful to everyone involved with this clinical trial.”

The first arm (Part A) of the PROSPECT Study is evaluating the safety and efficacy of tirabrutinib in patients with R/R PCNSL who received previous treatment with high-dose methotrexate-based regimens. Enrollment is now complete for Part A. ONO PHARMA continues to enroll newly diagnosed and previously untreated PCNSL patients in the second arm of the study (Part B), evaluating tirabrutinib in combination with one of two high-dose methotrexate-based regimens as first-line therapy in the PROSPECT Study (theprospectstudy.com and clinicaltrials.gov).

PCNSL is a rare and aggressive extranodal non-Hodgkin lymphoma with historically poor survival rates.[1] PCNSL affects the brain, its protective membranes, the spinal cord, and/or eye, without systemic involvement at the time of diagnosis.[1] 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.[2]

Tirabrutinib is a highly selective irreversible Bruton's tyrosine kinase inhibitor discovered by ONO PHARMA in Japan. In March 2023, the U.S. Food and Drug Administration granted Orphan Drug Designation to tirabrutinib for the treatment of PCNSL.[3] Tirabrutinib is currently approved for R/R PCNSL treatment in Japan, Taiwan, and South Korea.[3]

"This is an important milestone for ONO as it builds its clinical trial program in the U.S.,” said Kunihiko Ito, President and CEO of ONO PHARMA USA. “For decades, ONO’s commitment to innovation in oncology has helped change treatment paradigms for patients all over the world. We look forward to continuing this legacy as we investigate tirabrutinib for PCNSL in the U.S.”

**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 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. To learn more about R/R PCNSL, please visit navigatingpcnsl.com.

**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 a Phase 2 trial (NCT04947319) evaluating the safety and effectiveness of an investigational oral medicine called tirabrutinib for the potential treatment of newly diagnosed or relapsed/refractory (R/R) primary central nervous system lymphoma (PCNSL), 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 R/R 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: 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 https://us.ono-pharma.com.

**References**


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2. 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.
3. Tirabrutinib Receives Orphan Drug Designation From FDA. ONO Pharma USA, Inc. Accessed February 1, 2024. https://us.ono-pharma.com/news/tirabrutinib-receives-orphan-drug-designation



Contact:
Ono Pharmaceutical Co., Ltd.
Corporate Communications
public_relations@ono-pharma.com.

or

Laurie Casaday
ONO PHARMA USA
media_US@ono-pharma.com