ONO PHARMA

Press Release

# ONO PHARMA Presents Positive Results from Pivotal Trial in U.S. Patients with Relapsed or Refractory PCNSL at 2025 ASCO Annual Meeting

- *Primary central nervous system lymphoma (PCNSL) is a rare and aggressive lymphoma with no approved treatment in the U.S.*[1]
- *In the Phase 2 PROSPECT Study, tirabrutinib demonstrated an overall response rate of 67%, complete response rate of 44%, and a manageable safety profile*[2]

Osaka, Japan, May 28, 2025 - Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President and COO: Toichi Takino; "Ono") today announced that the results from the open label Phase 2 PROSPECT Study of tirabrutinib is to be presented at the 2025 American Society for Clinical Oncology (ASCO) annual meeting.[2] Patients in the U.S. with relapsed or refractory primary central nervous system lymphoma (R/R PCNSL) who received oral tirabrutinib as a monotherapy achieved an overall response rate (ORR) of 67%.[2]

Tirabrutinib is a highly selective irreversible, second generation Bruton's tyrosine kinase inhibitor discovered by Ono in Japan. In March 2023, the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation to investigational tirabrutinib for the treatment of PCNSL.[3]

"PCNSL is a rare and aggressive extranodal non-Hodgkin lymphoma with historically poor survival rates and no approved treatments in the U.S.," said Tracy Batchelor, MD, MPH, Mass General Brigham Chair of Neurology and Coordinating Investigator for the PROSPECT study. "The PROSPECT Study data show tirabrutinib provided a promising response rate in patients with R/R PCNSL, supporting its role as a potentially effective treatment option for patients living with this devastating disease."

## Study Results

In the PROSPECT Study, 48 patients with R/R PCNSL received oral tirabrutinib as a monotherapy once daily.[2,4] The primary endpoint was ORR, and secondary endpoints included duration of response (DOR), time to response (TTR), and safety.[2,4]

After a median follow-up of 11.5 months, ORR was 67%, with a complete response rate of 44%.[2] Median DOR was 9.3 months, and median TTR was 1.0 months.[2] Exploratory endpoints included median overall survival, which was not reached, and median progression-free survival, which was 6.0 months.[2]

Tirabrutinib demonstrated a generally favorable safety profile.[2] At data cutoff, 13 patients (27%) remained on tirabrutinib treatment.[2] The main reasons for discontinuation were disease progression (54.2%) and death (8.3%); one patient discontinued due to an adverse event (AE).[2] Incidence of grade ≥3 treatment-emergent adverse events (TEAEs) was 56.3%.[2] Any-grade treatment-related TEAEs were experienced by 75.0%, and most frequently included anemia (18.8%), rash maculo-papular (16.7%), fatigue (14.6%), neutrophil count decreased (14.6%), lymphocyte count decreased (14.6%), pruritus (14.6%), and rash (14.6%).[2] Two patients died of

TEAEs, which were considered unrelated to study treatment. [2]

“We are deeply grateful to the study investigators and the patients who participated in this study for making this important research possible,” said Thomas Lechner, MSc. Ph.D., VP, Medical Affairs, ONO PHARMA USA INC. “Tirabrutinib is approved for relapsed or recurring PCNSL in Japan, Taiwan, and South Korea and our hope is to bring this potential treatment to those living with this hard-to-treat disease in the U.S as soon as possible.”

PROSPECT Study data will be included in a regulatory submission to the FDA in the near future.

**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 immunocompromised 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. 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. It was subsequently approved for the treatment of Waldenstrom macroglobulinemia and lymphoplasmacytic lymphoma in August 2020.Tirabrutinib was approved for the treatment of relapsed or refractory PCNSL in South Korea in November 2021 and in Taiwan in February 2022.

**About the PROSPECT Study**

The PROSPECT Study is a Phase 2 trial (NCT04947319) evaluating the safety and efficacy 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 specifically approved in the U.S. for the treatment of PCNSL. Learn more about the PROSPECT

Study here: theprospectstudy.com.

**About ONO PHARMA USA INC.**

ONO PHARMA USA INC.(OPUS), established in 1998 as the U.S. subsidiary of Ono Pharmaceutical Co., Ltd., is pursuing the clinical development of new drug candidates in the U.S., from clinical development to regulatory approval and commercialization. In addition, OPUS is engaged in promotion of the discovery alliances and licensing activities to expand Ono's development pipeline and pursue the commercialization opportunities in the U.S. In February, 2025, Ono announced that it has reorganized the operations of its local subsidiaries in the U.S. in order to accelerate the expansion of its global presence. In line with the reorganization, key functions of OPUS, including US R&D and commercial and medical affairs are being integrated into Deciphera Pharmaceuticals, Inc. (Deciphera) in July 2025. Deciphera has robust and well-developed R&D capabilities and commercial presence in the U.S. and Europe. OPUS will remain as a center for research collaboration and licensing activities. For more information, please visit us.ono-pharma.com.

**References**

1. Schaff LR, Grommes C. Primary central nervous system lymphoma. *Blood*. 2022;140(9):971-979. doi:10.1182/blood.2020008377.

2. Nayak L, Grommes C, Kallam A, et al. Tirabrutinib for the treatment of relapsed or refractory primary central nervous system lymphoma: efficacy and safety from the phase II PROSPECT study. Presented at: 2025 American Society for Clinical Oncology (ASCO) meeting; May 30-June 3, 2025; Chicago, IL.

3. Tirabrutinib Receives Orphan Drug Designation From FDA. ONO PHARMA USA, Inc. Available from:https://us.ono-pharma.com/news/tirabrutinib-receives-orphan-drug-designation. Accessed February 2025.

4. ClinicalTrials.gov. Study of Tirabrutinib (ONO-4059) in Patients with Primary Central Nervous System Lymphoma (PROSPECT Study). Available from: https://clinicaltrials.gov/study/NCT04947319. Accessed February 2025.

**Contact**:

Ono Pharmaceutical Co., Ltd.

Corporate Communications

public_relations@ono-pharma.com