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Phase 2 Clinical Study Initiated for Velexbu (tirabrutinib), a BTK Inhibitor, in Patients with Primary Central Nervous System Lymphoma in the US

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; “ONO”) announced that it has initiated the Phase 2 clinical study in the US with Velexbu (tirabrutinib hydrochloride, Development code: ONO-4059) (“Velexbu”), a Bruton’s tyrosine kinase (“BTK”) inhibitor, in patients with primary central nervous system lymphoma (“PCNSL”).

This study is a multi-center, open-label, Phase 2 clinical study (PROSPECT study: ONO-4059-09) evaluating the efficacy, safety and pharmacokinetics of Velexbu in patients with PCNSL in the US. For more information, please visit the following website at [https://clinicaltrials.gov/ \(NCT04947319\)](https://clinicaltrials.gov/ (NCT04947319)).

ONO is committed to bringing a new treatment option to many PCNSL patients all over the world.

About Primary Central Nervous System Lymphoma (PCNSL)

PCNSL is a malignant lymphoma in which the lesion is localized in the cerebrospinal cord (including the eyes) at the first onset. It is estimated that there are approximately 980 new cases with PCNSL per year in Japan^{*1,2}. The signs and symptoms presented in patients with PCNSL vary depending on the site of the lesion, and include localized neuropathy, neuropsychiatric symptoms, symptoms associated with increased intracranial pressure, seizure, eye symptoms, headache, difficulty in movement, cranial neuropathy and radiculopathy.

Currently, untreated PCNSL patients receive high-dose methotrexate-based treatment followed by whole-brain radiation therapy, by which a certain patient population shows long-term remissions, but many patients will relapse. There are also refractory patients who do not respond to the initial treatment.

*1: Neurol Med Chir (Tokyo). 2017;57(Supplement 1):9-102.

*2: Jpn J Neurosurg VOL.24 NO.10 2015.10

About Velexbu

Velexbu, discovered and developed by ONO, is a highly selective, oral BTK inhibitor and has been developed for the treatment in patients with B-cell tumors and autoimmune diseases in Japan. B-cell receptor (BCR) signaling plays a core role in the survival, activation, proliferation, maturation and differentiation of B-cell lymphocyte. The BCR signaling pathway is known to be permanently activated particularly B cell non-Hodgkin lymphoma (B-NHL) and chronic lymphocytic leukemia (CLL). Velexbu is expected to have a therapeutic effect because it inhibits BTK, a mediator located downstream of BCR.

In Japan, Velexbu was approved in March 2020 and launched in May 2020 for the treatment of relapsed or refractory primary central nervous system lymphoma (PCNSL). Thereafter, Velexbu

was approved for additional indication of Waldenstrom macroglobulinemia (WM) and lymphoplasmacytic lymphoma (LPL) in Japan in August 2020.

Outside of the Oncology field, ONO is conducting clinical studies for the treatment of pemphigus (Phase 2) and generalized scleroderma (Phase 1).

Contact:

Ono Pharmaceutical Co., Ltd.

Corporate Communications

public_relations@ono.co.jp