ONO PHARMACEUTICAL CO.,LTD.

February 21, 2022

Velexbru® Tablet 80 mg, a BTK inhibitor, Approved in Taiwan for the Treatment of Recurrent or Refractory B-cell Primary Central Nervous System Lymphoma

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director: Gyo Sagara; "ONO") announced today that Ono Pharma Taiwan Co., Ltd. ("OPTW"), a Taiwanese subsidiary of ONO, received an approval of Velexbru® (generic name: tirabrutinib hydrochloride) Tablet 80 mg ("Velexbru"), a Bruton's tyrosine kinase ("BTK") inhibitor, on February 18 in Taiwan from the Taiwan Food and Drug Administration (TFDA) for the treatment of adult patients with recurrent or refractory B-cell primary central nervous system lymphoma.

This approval is based on the results from a multi-center, open-label, uncontrolled Phase I/II study (ONO-4059-02), conducted in Japan, evaluating an efficacy and safety of Velexbru in patients with recurrent or refractory primary central nervous system lymphoma (PCNSL). In this study, the overall response rate (ORR) assessed by an independent review committee (IRC), a primary endpoint, was 52.9% (9/17 patients) in patients who received 480 mg of Velexbru in the fasting which is the approved dosage and administration this time. The major Grade 3 - 4 adverse drug reactions were neutropenia, leucopenia and hypertriglyceridemia which occurred each in 11.8% (2/17 patients).

This approval represents that Velexbru is the first BTK inhibitor approved in Taiwan for the treatment of adult patients with recurrent or refractory B-cell PCNSL for which no standard of care has been established.

About ONO-4059-02 Study

This study is a multi-center, open-label, uncontrolled Phase I/II study, conducted in Japan, evaluating the efficacy and safety of Velexbru monotherapy in patients with recurrent or refractory PCNSL. In this study, 44 patients were recruited and received Velexbru 320 mg (20 patients), 480 mg (7 patients) and 480 mg in the fasting (17 patients), orally, once a day in each group. Patients were treated until disease progression or unacceptable toxicity was observed. The primary endpoint of this study is ORR assessed by the independent review committee (IRC).

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. The signs and symptoms presented by 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, previously 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 drug treatment. Standard treatment has not been established for patients with recurrent or

refractory PCNSL, and treatment options are limited for them. Therefore, a new treatment drug was expected for this patient population.

About Velexbru

Velexbru is a highly selective, oral Bruton's tyrosine kinase (BTK) inhibitor. 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 in B-cell non-Hodgkin lymphoma (B-NHL) and chronic lymphocytic leukemia (CLL). Velexbru is expected to have a therapeutic effect because it inhibits BTK, a mediator located downstream of BCR.

In Japan, ONO received a manufacturing and marketing approval of Velexbru in March 2020 and launched it in May 2020 for the treatment of relapsed or refractory primary central nervous system lymphoma (PCNSL). Thereafter, ONO received the approval of Velexbru for additional indication of Waldenstrom macroglobulinemia (WM) and lymphoplasmacytic lymphoma (LPL) in August 2020. Outside of the oncology field, ONO is conducting clinical studies for the treatment of pemphigus (Phase II) and generalized scleroderma (Phase I).

About Ono Pharma Taiwan Co., Ltd.

Ono Pharma Taiwan Co., Ltd. (Taipei, Taiwan, "OPTW") is an ONO's wholly-owned subsidiary established in December 2014. OPTW has established its own sales organization in Taiwan and marketed Opdivo, an anti-PD-1 antibody/anti-neoplastic drug since 2016. OPTW is committed to bringing more innovative new products to meet unmet medical needs to patients in Taiwan as soon as possible.

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