ONO PHARMACEUTICAL CO.,LTD.

November 8, 2021

Velexbru® Tablet 80 mg, a BTK inhibitor, Approved in South Korea for 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 Korea Co., Ltd. ("OPKR"), a South Korean subsidiary of ONO, received a marketing approval of Velexbru® (generic name: tirabrutinib hydrochloride) Tablet 80 mg ("Velexbru"), a Bruton's tyrosine kinase ("BTK") inhibitor, on November 5, 2021 from the Ministry of Food and Drug Safety (MFDS) in South Korea for the treatment of 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) of patients.

This approval represents that Velexbru is the first BTK inhibitor approved in South Korea for the treatment of 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, 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 fasted (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 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, 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 is 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 Korea Co., Ltd.

Ono Pharma Korea Co., Ltd. (OPKR), in Seoul, Korea, was established as a wholly-owned subsidiary of ONO in December 2013. OPKR has marketed specialty products such as anti-cancer agent, including Opdivo, an anti-PD-1 antibody. OPKR has been committed to developing and marketing its products created internally for further penetration into the South Korean market.

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