ONO PHARMA

Press Release

Ono Pharma Submits a Supplemental Application in Japan to Expand the Use of VELEXBRU® Tablets for the Treatment of Central Nervous System Involvement of Malignant Lymphoma in Patients with Inadequate Response to Existing Therapies or in Whom Such Therapies Are Not Appropriate

- Supplemental Application was submitted in Japan for a partial change in the manufacturing and marketing approval of VELEXBRU for the indication of central nervous system involvement of malignant lymphoma in patients with inadequate response to existing therapies or in whom such therapies are not appropriate.
- Standard-of-care treatment has not been established for this indication, and there is a strong need for a new therapeutic option.
- This application is based on the results of a phase 2 investigator-initiated trial.

Osaka, Japan, June 11, 2026—Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President and COO: Toichi Takino; "Ono") today announced that it submitted a supplemental application of VELEXBRU® Tablets 80mg (generic name, tirabrutinib hydrochloride; "VELEXBRU"), a Bruton's tyrosine kinase (BTK) inhibitor in Japan, to expand its use for the treatment of central nervous system involvement of malignant lymphoma in patients with inadequate response to existing therapies or in whom such therapies are not appropriate for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the results of a phase 2 investigator-initiated trial (NCCH2201/MK013 trial, the CRYSTAL trial) conducted at multiple centers in Japan, including the National Cancer Center Hospital, involving patients with relapsed or refractory secondary central nervous system lymphoma (SCNSL).

SCNSL is a pathological condition in which systemic malignant lymphoma infiltrates the central nervous system (CNS)[1,2] and is distinct from primary central nervous system lymphoma (PCNSL), in which lesions are confined to the CNS at initial onset. In SCNSL, depending on the sites of lesions, patients may experience focal neurological symptoms such as cranial nerve palsy, weakness in the arms and legs, and visual symptoms, as well as symptoms associated with intracranial hypertension such as headache, nausea/vomiting, and psychiatric symptoms including apathy.[3]
In Japan, high-dose methotrexate-based pharmacotherapy is currently used for SCNSL.[4,5] However, a standard-of-care treatment has not been established for patients with inadequate response, including relapse after treatment, to existing therapies or in whom such therapies are not appropriate, and there is a strong need for a new therapeutic option.

VELEXBRU was designated as an orphan drug for the indication of central nervous system involvement of malignant lymphoma in patients with inadequate response to existing therapies or in whom such therapies are not appropriate on May 18, 2026 and is accepted for priority review by the Ministry of Health, Labour and Welfare (MHLW).

About NCCH2201/MK013 Trial (CRYSTAL Trial)

The NCCH2201/MK013 trial is an investigator-initiated, multi-center, open-label, uncontrolled phase 2 clinical trial designed to evaluate the efficacy and safety of VELEXBRU monotherapy in

patients with relapsed or refractory SCNSL. The primary endpoint is objective response rate (central review). Secondary endpoints include objective response rate (investigator assessment), progression-free survival, overall survival, duration of response, and others. The results from this trial will be presented at the European Hematology Association (EHA) 2026 congress to be held in Stockholm, Sweden, from June 11 to June 14, 2026.

This trial was conducted as a sub-study of the MASTER KEY Project*, an industry-academia collaborative initiative led by the National Cancer Center Hospital in Japan to promote treatment development for rare cancers.

*https://www.ncc.go.jp/jp/ncch/masterkeyproject/index.html

About VELEXBRU

VELEXBRU is a highly selective oral BTK inhibitor discovered by Ono. B-cell receptor (BCR) signaling plays a core role in the survival, activation, proliferation, maturation, and differentiation of B-cell lymphocyte.

In Japan, Ono obtained approval in March 2020 for the indication of relapsed or refractory primary central nervous system lymphoma and launched VELEXBRU® Tablets in May 2020. Thereafter, Ono obtained an approval for additional indications in Japan in August 2020 for Waldenstrom macroglobulinemia and lymphoplasmacytic lymphoma. In South Korea, Ono obtained approval in November 2021, and in Taiwan in February 2022, for relapsed or refractory primary central nervous system lymphoma. In the United States, a New Drug Application for tirabrutinib for relapsed or refractory primary central nervous system lymphoma was accepted for filing in February 2026.

References:

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