ONO PHARMACEUTICAL CO.,LTD.

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ONO Submits Supplemental Application of Kyprolis® for Intravenous Injection, a Proteasome Inhibitor, for Additional Dosage and Administration for the Treatment of Relapsed or Refractory Multiple Myeloma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that ONO submitted a supplemental application of Kyprolis® for Intravenous Injection 10mg and 40mg (generic name: carfilzomib; "Kyprolis"), a proteasome inhibitor, in Japan for additional dosage and administration for the treatment of relapsed or refractory multiple myeloma, as a partial change in approved items of the manufacturing and marketing approval.

This application is based on the result from a global multiple-center, randomized, open-label Phase 3 study (ONO-7057-06/A.R.R.O.W. study), evaluating the efficacy and safety of Kyprolis in combination with dexamethasone, comparing Kyprolis 20/70 mg/m^2 once-weekly dosing regimen versus Kyprolis 20/27 mg/m^2 twice-weekly regimen in patients with relapsed or refractory multiple myeloma. In this study, Kyprolis administered once-weekly at 20/70 mg/m^2 with dexamethasone demonstrated statistically superior progression-free survival (PFS) compared with twice-weekly 20/27 mg/m^2. The safety profile of these 2 arms was similar and no new safety concern was observed in once-weekly arm.

Kyprolis was granted a manufacturing and marketing approval for the treatment of relapsed or refractory multiple myeloma in Japan in July 2016, in combination with lenalidomide and dexamethasone at a dosage of 20 mg/m^2 (body surface area) in Cycle 1 on Day 1 and 2, and escalate to 27 mg/m^2 twice a week thereafter. Further, Kyprolis was approved for additional dosage and administration in combination with dexamethasone at a dosage of 20 mg/m^2 only in Cycle 1 on Day 1 and 2, and escalate to 56 mg/m^2 twice a week thereafter.

With the current dosage and administration, Kyprolis should be given twice a week. This application is intended to expand additional dosage and administration in combination with dexamethasone at a dosage of 20 mg/m^2 only in Cycle 1 on Day 1, and escalate to 70 mg/m^2 once a week thereafter.

Multiple myeloma results from an abnormality of plasma cells, usually in the bone marrow and there are nearly 18,000 patients* in Japan. Several regimens for multiple myeloma are currently available to patients. However, the disease relapses and progresses and eventually becomes no longer responding to therapies, also known as refractory disease. Additionally, adverse drug reactions and co-morbid conditions have been reported following long-term treatment, making continued treatment a challenge.

Kyprolis is in a class of drugs called proteasome inhibitors. ONO licensed-in Kyprolis for development and commercialization in Japan in September 2010 from US-based Onyx Pharmaceuticals, Inc., now an Amgen subsidiary. Proteasome, an intra-cellular enzyme complex, functions to mediate degradation of polyubiquitinated proteins and control proliferation and differentiation of cells, as well as functional cell-death. Kyprolis inhibits certain proteasome activity, thereby inducing functional cell-death of myeloma.

Since Kyprolis was first approve for the treatment of patients with multiple myeloma in the US in July 2012, approximately 80,000 patients worldwide have received Kyprolis. As for the dosage and administration of Kyprolis 20/70 mg/m^2 once-weekly filed in Japan this time, it was approved in the US in September 2018.

*: Vital Statistics and Patients Survey, 2014 (Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare).

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