News Release

FDA Approves VELCADE® (bortezomib) Retreatment in Patients with Multiple Myeloma

Cambridge, Mass., August 8, 2014 – Millennium: The Takeda Oncology Company with its parent company, Takeda Pharmaceutical Company Limited (TSE:4502), today announced that the U.S. Food and Drug Administration (FDA) has approved VELCADE® (bortezomib) for the retreatment of adult patients with multiple myeloma (MM) who had previously responded to VELCADE therapy and relapsed at least six months following completion of prior VELCADE treatment. The labeling update includes dosing guidelines as well as safety and efficacy findings for the use of VELCADE as a single agent or VELCADE in combination with dexamethasone in patients previously treated with VELCADE. VELCADE retreatment may be started at the last tolerated dose.

The approved retreatment sNDA consisted of a Phase 2 study and other supportive data. The Phase 2 international RETRIEVE trial showed a 38.5 percent overall response rate (ORR) in multiple myeloma patients who had been previously treated with a VELCADE-based regimen (median of two prior lines of therapy) and had previously achieved a partial response or better. The safety profile seen with VELCADE retreatment was consistent with the known safety profile of intravenous VELCADE in relapsed multiple myeloma; no cumulative toxicities were observed upon retreatment. The most common adverse drug reaction was thrombocytopenia, which occurred in 52 percent of the patients.

“For the past 11 years, VELCADE has played an important role as the only therapy proven to extend overall survival for patients with newly diagnosed and relapsed multiple myeloma,” said Michael Vasconcelles, MD, Global Head, Oncology Therapeutic Area Unit, Takeda. “With these newly approved dosing guidelines, physicians will be able to provide their patients, who have previously received VELCADE, with an effective treatment extending VELCADE use across the continuum of care of multiple myeloma.”

RETRIEVE was a single arm, open-label trial. The study enrolled 130 patients ages 18 years and older who had previously responded to VELCADE-based therapy and relapsed at least six months after prior treatment with VELCADE. The study met its primary endpoint of best confirmed response to retreatment as assessed by European Group for Blood and Marrow Transplantation (EBMT) criteria.

- Patients had received a median of two prior therapies (range of 1-7).
- Dexamethasone was administered in combination with VELCADE in 94 patients.
- Of the 130 patients, one patient achieved complete response and 49 achieved partial response (50/130; ORR 38.5 percent).
- In the 50 responding patients, the median duration of response was 6.5 months (range of 0.6 to 19.3 months).
- The incidence of grade ≥3 thrombocytopenia was 24 percent. Peripheral neuropathy occurred in 28 percent of patients, with the incidence of grade ≥3 peripheral neuropathy reported at 6 percent. The incidence of serious adverse reactions was 12.3 percent; the most commonly reported serious adverse reactions were thrombocytopenia (3.8 percent), diarrhea (2.3 percent), herpes zoster and pneumonia (1.5 percent each). Adverse reactions leading to discontinuation occurred in 13 percent of patients.

VELCADE: Important Safety Information

VELCADE® (bortezomib) is approved for the treatment of patients with multiple myeloma. VELCADE is also approved for the treatment of patients with mantle cell lymphoma who have already received at least one prior treatment.

Patients should not receive VELCADE if they are allergic to bortezomib, boron or mannitol. VELCADE should not be administered intrathecally. Women should avoid becoming pregnant or breastfeeding while taking VELCADE. Patients with diabetes may require close monitoring and adjustment of their medication. VELCADE can cause serious side effects, including:

- ***Peripheral neuropathy*****.** Nerve problems, which can be severe including muscle weakness, tingling, burning, pain, or loss of feeling in the hands and feet.
- ***Low blood pressure.*** A drop in blood pressure resulting in dizziness, light headedness or fainting.
- ***Heart problems.*** Heart rhythm problems and heart failure including worsening of existing conditions. Symptoms may include chest pressure or pain, palpitations, swelling of the ankles or feet, or shortness of breath.
- ***Lung problems,*** some of which have been fatal. Symptoms include cough, shortness of breath, wheezing or difficulty breathing.
- ***Liver problems.*** Liver failure including a yellow discoloration of the eyes and skin.
- ***Posterior reversible encephalopathy syndrome (PRES***). A rare, reversible condition involving the brain. Symptoms may include seizures, high blood pressure, headaches, tiredness, confusion, blindness, or other vision problems
- ***Gastrointestinal problems.*** Nausea, vomiting, diarrhea and constipation.
- ***Thrombocytopenia and neutropenia*****.** Lowering the levels of blood cells, which could result in a higher risk for infections or bleeding.
- ***Tumor lysis syndrome (TLS).*** TLS is a syndrome that causes a chemical imbalance in the blood that could lead to heart and/or kidney problems.

Common side effects seen in patients receiving VELCADE include: fever, decreased appetite, fatigue, rash.

These are not all of the possible side effects with VELCADE. Please see the full Prescribing Information for VELCADE for a complete list available at VELCADE.com.

About VELCADE®

VELCADE® (bortezomib) is co-developed by Millennium/Takeda and Janssen Pharmaceutical Companies. Millennium is responsible for commercialization of VELCADE in the U.S.; Janssen Pharmaceutical Companies are responsible for commercialization in Europe and the rest of the world. Takeda Pharmaceutical Company Limited and Janssen Pharmaceutical K.K. co-promote VELCADE in Japan. VELCADE is approved in more than 90 countries and has been used to treat more than 550,000 patients worldwide.

About Millennium: The Takeda Oncology Company

Millennium: The Takeda Oncology Company, a leading biopharmaceutical company based in Cambridge, Mass., markets a first-in-class proteasome inhibitor and has a robust pipeline of oncology product candidates. Additional information about Millennium is available through its website, www.millennium.com.

About Takeda

Located in Osaka, Japan, Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for patients worldwide through leading innovation in medicine. Additional information about Takeda is available through its corporate website, www.takeda.com.

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Editors' Note: This press release is also available under the Media section of the Company's website at: www.millennium.com/InTheNews.aspx.

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