Better Health, Brighter Future

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# News Release

## NEW TREATMENT OPTION FOR CANADIANS LIVING WITH MULTIPLE MYELOMA

*Takeda Canada receives approval for NINLARO™ (ixazomib) - the first and only oral proteasome inhibitor providing a new disease management option for adult patients living with incurable cancer*

**OAKVILLE, Ontario – August 8, 2016** – Takeda Canada has received approval from Health Canada for NINLARO™ (ixazomib) in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy[i]. NINLARO™ is the first and only oral proteasome inhibitor, and the approval makes a new option available to meet the urgent needs of patients living with relapsed and/or refractory multiple myeloma, a devastating, rare, relapsing and incurable cancer.

NINLARO™ was developed to address patient needs and overcome some of the significant burdens they face. Current administration of IV/injectable therapies typically occur in-clinic or in-hospital for most patients requiring significant travel and time constraints. With availability in Canada expected shortly, NINLARO™'s once-weekly oral dosing provides flexibility and choice for Canadians managing relapsed and/or refractory multiple myeloma. Following the U.S. Food and Drug Administration approval in November 2015, Canada is the second country in the world to approve NINLARO™.

Aldo Del Col, Co-founder and Chairman of the Board of Myeloma Canada said, "Multiple myeloma, while treatable, remains largely incurable. Patients urgently need new and effective treatments that offer hope for delaying disease progression when the currently approved myeloma therapies no longer work. I'm pleased to see with the approval of NINLARO™, we now have another treatment option for Canadians living with multiple myeloma."

Due to the unmet need in this patient population, the New Drug Submission for NINLARO™ was granted a Priority Review by Health Canada. Takeda is committed to making NINLARO™ available and accessible for myeloma patients in Canada and will consider offering specialised programs, enabling patients to receive rapid access to medicine, quality care, and ongoing support along their treatment journey in multiple myeloma.

"Multiple myeloma, a devastating diagnosis for patients and their families, is a complicated disease that requires effective treatment options," said Dr. Donna Reece, Professor and Director of the Program for Multiple Myeloma and Related Diseases in the Department of Medical Oncology and Haematology at Princess Margaret Hospital/University of Toronto. "The approval of NINLARO™ offers a much-needed new option for Canadian patients with multiple myeloma who have received at least one prior therapy. Its oral delivery may help multiple myeloma patients overcome some of the logistical burdens they may face with current therapies, which are typically administered in-clinic or in-hospital requiring significant travel and time constraints."

“Health Canada’s approval of NINLARO™ represents an important step in Takeda’s unwavering commitment to combat cancer by delivering novel therapies to patients as quickly, effectively and safely as possible,” says Chatrick Paul, General Manager at Takeda Canada. “We are the second country in the world to gain approval to deliver NINLARO™ as a critical treatment option for multiple myeloma patients. We are pleased that NINLARO™ – our first oncology prescription medicine in Canada – has a product label that is broad and robust, meaning Canadians living with multiple myeloma will now have a highly effective treatment option available to them in the comfort of their home, making their road to survival with this chronic disease more liveable.”

**About the TOURMALINE-MM1 Trial**

TOURMALINE-MM1 is an international, randomized, double-blind, placebo-controlled clinical trial of 722 patients, designed to evaluate NINLARO™ plus lenalidomide and dexamethasone compared to placebo plus lenalidomide and dexamethasone in adult patients with relapsed and/or refractory multiple myeloma. Results showed that when combined with lenalidomide and dexamethasone, NINLARO™ is effective in extending Progression Free Survival (PFS) over lenalidomide and dexamethasone alone and has a manageable safety profile. The trial achieved its primary endpoint and demonstrated a clinically meaningful and statistically significant prolongation in PFS at this analysis, which showed that patients treated in the NINLARO™ arm lived without their disease worsening for a significantly longer time compared to patients in the control arm. Patients continue to be treated to progression in this trial and will be evaluated for long term outcomes.

In the TOURMALINE-MM1 trial, the most common adverse reactions (≥20%) in patients receiving NINLARO™ included diarrhea, constipation, thrombocytopenia, peripheral neuropathy, nausea, peripheral edema, vomiting and back pain. Serious adverse reactions reported in ≥2% patients included thrombocytopenia (2%) and diarrhea (2%)[i].

Efficacy and safety data were reviewed by an Independent Data Monitoring Committee (IDMC), who recommended the study be continued in a blinded fashion to allow further maturation of long term outcomes, including overall survival (OS) and long-term safety.

**About NINLARO™ (ixazomib) capsules**

NINLARO™ is an oral proteasome inhibitor. Proteasomes play an important role in cells by breaking down unwanted proteins. NINLARO™ blocks proteasomes from working and causes a build-up of proteins in cells. This can cause cell death, especially in multiple myeloma cells because they are more likely to contain a higher amount of abnormal proteins. NINLARO™ is approved in combination with lenalidomide and dexamethasone, to treat adults with multiple myeloma who have received at least one prior multiple myeloma treatment[i].

NINLARO™ is administered orally, once-weekly on days 1, 8, and 15 of a 28-day treatment cycle. NINLARO™ received a priority approval in the U.S. and has also received Breakthrough Therapy status by the U.S. FDA for relapsed or refractory systemic light-chain (AL) amyloidosis, a related ultra orphan disease, in 2014. NINLARO™ is currently under review by the European Medicines Agency (EMA) and was granted an accelerated assessment by the Committee for Medicinal Products for Human Use (CHMP).

The TOURMALINE clinical development program further reinforces Takeda’s ongoing commitment to developing innovative therapies for people living with multiple myeloma worldwide and the healthcare professionals who treat them. Five global Phase 3 trials are ongoing:

- TOURMALINE-MM1, investigating ixazomib vs. placebo, in combination with lenalidomide and dexamethasone in relapsed and/or refractory multiple myeloma
- TOURMALINE-MM2, investigating ixazomib vs. placebo, in combination with lenalidomide and dexamethasone in patients with newly diagnosed multiple myeloma
- TOURMALINE-MM3, investigating ixazomib vs. placebo as maintenance therapy in patients with newly diagnosed multiple myeloma following induction therapy and autologous stem cell transplant (ASCT)
- TOURMALINE-MM4, investigating ixazomib vs. placebo as maintenance therapy in patients with newly diagnosed multiple myeloma who have not undergone ASCT
- TOURMALINE-AL1, investigating ixazomib plus dexamethasone vs. physician choice of selected regimens in patients with relapsed or refractory AL amyloidosis

In addition to the TOURMALINE program, a large number of investigator initiated studies are evaluating ixazomib for patients globally.

**About Multiple Myeloma**

Multiple myeloma is a cancer of the plasma cells, which are found in the bone marrow. In multiple myeloma, a group of plasma cells, or myeloma cells, becomes cancerous and multiplies, increasing the number of plasma cells to a higher than normal level. Because plasma cells circulate widely in the body, they have the potential to affect many bones in the body, possibly resulting in compression fractures, lytic bone lesions and related pain. Multiple myeloma can cause a number of serious health problems affecting the bones, immune system, kidneys and red blood cell count, with some of the more common symptoms including bone pain and fatigue, a symptom of anaemia. Multiple myeloma is a rare form of cancer. In Canada, it is estimated that approximately 7,500 people live with multiple myeloma, with 2,700 new cases estimated to be diagnosed in 2015[ii].

**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 people worldwide through leading innovation in medicine. Additional information about Takeda is available at takeda.com.

**Takeda Canada**, located in Oakville, Ontario, is the Canadian sales and marketing organization of Takeda Pharmaceutical Company Limited. Takeda Canada is transforming to become an agile specialty pharmaceutical company, focusing on gastroenterology and oncology, while continuing to meet a number of important primary care needs. Additional information about Takeda Canada is available at takedacanada.com.

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[i] NINLARO™ Product Monograph. Takeda Canada Inc. (August 2016)
[ii] Canadian Cancer Statistics 2015