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Health Canada Approves KEYTRUDA® (pembrolizumab) as First-line Treatment for Adults with Metastatic Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer

Approval Based on Significant Progression Free Survival Findings from Phase 3 KEYNOTE-177 Trial

- KEYTRUDA® is an anti-PD-1 therapy that works by helping increase the ability of the body's immune system to help detect and fight tumour cells.¹
- An estimated 26,900 Canadians were diagnosed with colorectal cancer in 2020, with an average of 73 Canadians diagnosed daily.²

KIRKLAND, QC – March 8, 2021 - Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that Health Canada has approved KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, for the first-line treatment, as monotherapy, for adult patients with metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).³

"This approval offers a new first-line treatment option for patients with MSI-H/dMMR metastatic colorectal cancer," said Dr. Ron Burkes, Professor of Medicine, University of Toronto and Medical Oncologist, Mount Sinai Hospital.

Colorectal cancer, one of the most commonly diagnosed cancers in Canada, occurs when abnormal cells in the colon or rectum develop into benign tumours that, over time, transform into cancerous tumours that can spread to the blood and lymph vessels and metastasize.^{4,5} In 2020, an estimated 26,900 Canadians were diagnosed with CRC, with an average of 73 Canadians diagnosed daily.⁶ In Canada, it is the second leading cause of death from cancer in men and the third leading cause of death from cancer in women.⁷ Approximately three to five per cent of CRCs are associated with a hereditary cancer predisposition related to deoxyribonucleic acid (DNA) mismatch repair (MMR)

deficiency. Mismatch repair is a process that corrects mismatches generated during DNA replication, recombination, and damage. Deficient mismatch repair (dMMR) causes an inability to correct DNA replication errors, allowing mutations to continue throughout the genome, particularly in regions of repetitive DNA known as microsatellite, which can lead to MSI-H.⁸

“This is excellent news for colorectal cancer patients with MSI-H/dMMR tumours,” says Barry D. Stein, a colon cancer survivor and president of Colorectal Cancer Canada. “This drug is encouraging because it can help some patients achieve a better quality of life and more time with family and loved ones. Innovative treatment options, like this one, are helping to make a difference for Canadians facing this particular colon cancer.”

About KEYNOTE-177 Trial

Health Canada’s approval for CRC is based on findings from the Phase 3 study KEYNOTE-177, a multicenter, randomized, open-label, active-controlled trial conducted in 307 patients with previously untreated metastatic MSI-H or dMMR CRC.⁹ Patients were randomized 1:1 to receive 200 milligrams (mg) of KEYTRUDA® intravenously every three weeks or chemotherapy regimens given intravenously every two weeks.¹⁰

The results of KEYNOTE-177 showed that KEYTRUDA® demonstrated a statistically significant improvement in progression free survival (PFS) compared to patients treated with chemotherapy.¹¹ The median PFS in patients treated with KEYTRUDA® was 16.5 months compared to 8.2 months in the chemotherapy arm (HR=0.60 [95% CI, 0.45-0.80]; p=0.0002).¹² The average objective response rate (ORR) for the KEYTRUDA® arm was 44% compared to 33% in the chemotherapy arm, and the average duration of response at 24 months was 83% in the KEYTRUDA® arm versus 35% in the chemotherapy arm.¹³

“The approval of KEYTRUDA® as a first-line treatment for metastatic MSI-H or dMMR colorectal cancer marks its nineteenth indication, reinforcing Merck’s ongoing commitment to science and to the research and development in immuno-oncology,” says Anna Van Acker, President, Merck Canada. “We hope that this new treatment option will have a meaningful impact for those Canadians who live with MSI-H/dMMR colorectal cancer. We are devoted to our straightforward mission and to continue all relentless efforts to help more Canadians living with cancer.”

About Colorectal Cancer

Colorectal cancer occurs when the cells lining the rectum or colon become abnormal and begin to divide rapidly, resulting in the development of benign tumours.¹⁴ Over time, the DNA of the benign tumours can change, causing the tumours to become cancerous.¹⁵ This can result in the cancer spreading to the blood and lymph vessels, further allowing it to metastasize and reach other organs such as the lungs or liver.¹⁶ Since there is no clear border between the colon and rectum and they are made of the same tissues, they are categorized together as CRC.¹⁷ As most CRC cases are related to aging, over 90% of cases occur in patients over the age of 50.¹⁸ Over half (56%) of CRC cases are expected to occur in Canadians who fall within the age covered by Canadian screening guidelines (50 to 74 years), while approximately 7% of colorectal cancer cases are expected to be diagnosed in people younger than 50 years of age.¹⁹

About KEYTRUDA®

KEYTRUDA® is an anti-PD-1 therapy that works by helping increase the ability of the body's immune system to help detect and fight tumour cells.²⁰ KEYTRUDA® is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumour cells and healthy cells.²¹

KEYTRUDA® was first approved in Canada in 2015 and currently has 19 indications in several disease areas, including advanced renal cell carcinoma (RCC), bladder cancer, non-small cell lung carcinoma (NSCLC), classical Hodgkin lymphoma (cHL), melanoma and head and neck squamous cell carcinoma (HNSCC).²²

Merck's Research Program

Merck has the industry's largest immuno-oncology clinical research program. There are currently more than 750 trials studying pembrolizumab across a wide variety of cancers and treatment settings. This clinical program seeks to understand the role of pembrolizumab across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with this medication, including exploring several different biomarkers.

Our Focus on Cancer

Our goal is to translate progressive science into innovative oncology medicines to help people with cancer worldwide. At Merck Oncology, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in

immuno-oncology and we are accelerating every step in the journey — from lab to clinic — to potentially bring new hope to people with cancer.

About Merck

For more than 125 years, Merck, known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals — including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases — as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information about our operations in Canada, visit www.merck.ca and connect with us on [YouTube](#) and [Twitter](#).

Forward-Looking Statement of Merck & Co. Inc., Kenilworth, NJ, USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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Please see the product monograph for KEYTRUDA® (pembrolizumab) at:

https://www.merck.ca/static/pdf/KEYTRUDA-PM_E.pdf.

References

¹ KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

² Canadian Cancer Society. Colorectal Cancer Statistics. Available at <https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/statistics/?region=on>. Accessed on March 4, 2021.

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⁴ Canadian Cancer Society. Colorectal Cancer Statistics. Available at <https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/statistics/?region=on>. Accessed on March 4, 2021.

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⁹ KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

¹⁰ KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

¹¹ KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

¹² KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

¹³ KEYTRUDA® Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

¹⁴ Colorectal Cancer Canada. Colorectal Cancer. Available at <https://www.colorectalcancerCanada.com/colorectal-cancer/what-is-colorectal-cancer/>. Accessed on March 4, 2021.

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¹⁶ Colorectal Cancer Canada. Colorectal Cancer. Available at <https://www.colorectalcancerCanada.com/colorectal-cancer/what-is-colorectal-cancer/>. Accessed on March 4, 2021.

¹⁷ Canadian Cancer Society. What is Colorectal Cancer? Available at <https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/colorectal-cancer/?region=on#:~:text=Colorectal%20cancer%20starts%20in%20the,intestine%20and%20the%20digestive%20system>. Accessed on March 4, 2021.

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¹⁹ Government of Canada. Canadian Cancer Society. Canadian Cancer Statistics 2019. Available at <https://www.cancer.ca/~media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2019-EN.pdf?la=en>. Accessed on March 4, 2021.

²⁰ KEYTRUDA[®] Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

²¹ KEYTRUDA[®] Product Monograph. Merck & Co. Inc. Updated March 3, 2021.

²² KEYTRUDA[®] Product Monograph. Merck & Co. Inc. Updated March 3, 2021.