Merck KGaA
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News Release

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Merck KGaA, Darmstadt, Germany's Cladribine Tablets Approved for Relapsing-Remitting Multiple Sclerosis in Canada

- **First oral short-course treatment for relapsing- remitting multiple sclerosis (RRMS) now approved in Canada, with one of the highest rates of MS in the world[1]**
- **Cladribine Tablets has shown sustained clinical efficacy with a duration of oral treatment of 20 days over 2 years**
- **The approval of Cladribine Tablets by Health Canada follows the recent approval of Cladribine Tablets across Europe by the European Commission**

Darmstadt, Germany, December 4, 2017 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced today that Health Canada has approved MAVENCLAD™ (Cladribine Tablets) as monotherapy for the treatment of adult patients with relapsing-remitting multiple sclerosis (RRMS) to reduce the frequency of clinical exacerbations and delay the progression of disability. Cladribine Tablets is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, one or more therapies for multiple sclerosis.[2]. Cladribine Tablets is the first and only oral short-course treatment to provide efficacy across key measures of disease activity in patients with RRMS, including disability progression, annualized relapse rate and magnetic resonance imaging (MRI) activity.

"Cladribine Tablets is a unique new treatment for our patients that offers potent efficacy with only 20 days of oral treatment over two years," said Dr. Mark S. Freedman, Director, Multiple Sclerosis Research Unit at the Ottawa Hospital, Senior

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Scientist at The Ottawa Hospital Research Institute and investigator for the CLARITY study.

“Health Canada's approval of Cladribine Tablets represents a significant milestone,” said Rehan Verjee, EVP, Chief Marketing and Strategy Officer at the biopharma business of Merck KGaA, Darmstadt, Germany. “We are exceptionally proud of our long-standing partnership with the MS community in Canada and would like to thank the many Canadian patients and investigators who have supported the development of Cladribine Tablets.”

Cladribine Tablets are thought to work by selectively targeting B & T lymphocytes followed by lymphocyte reconstitution.**Fehler! Textmarke nicht definiert.**

The Health Canada Notice of Compliance follows the European Commission (EC) marketing authorization received in August 2017. Product availability in Canada is expected in early January 2018. Merck KGaA, Darmstadt, Germany, plans additional filings for regulatory approval in other countries, including the United States.

About Cladribine Tablets
Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes thought to be integral to the pathological process of relapsing MS (RMS). Cladribine Tablets is currently under clinical investigation and not yet approved for any use in the United States.
In August 2017, the European Commission (EC) granted marketing authorization for Cladribine Tablets, marketed as MAVENCLAD®, for the treatment of adult patients with highly active relapsing forms of multiple sclerosis (RMS) as defined by clinical or imaging features in the 28 countries of the European Union (EU) in addition to Norway, Liechtenstein and Iceland. In December 2017, Cladribine Tablets, marketed as MAVENCLAD™ was approved in Canada for relapsing-remitting multiple sclerosis (RRMS). Cladribine Tablets is currently under clinical investigation and not yet approved for the treatment for any use in the United States.

The clinical development program for Cladribine Tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a two-year Phase III placebo-controlled study following on from the CLARITY study, designed to evaluate the safety and efficacy of Cladribine Tablets over an extended administration for four years.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).
- The ONWARD (Oral Cladribine Added ON To Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding Cladribine Tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis Patients Who Have Participated in Cladribine Clinical Studies) study: interim long-term follow-up data from the prospective registry, PREMIERE, to evaluate the safety and efficacy of Cladribine Tablets

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The clinical development program of Cladribine Tablets in MS comprises more than 10,000 patient years of data with over 2,700 patients included in the clinical trial program, and more than 10 years of observation in some patients.

About Multiple Sclerosis (MS)
Multiple sclerosis (MS) is an autoimmune, chronic and inflammatory condition that affects the central nervous system (CNS) and is the most common, non-traumatic, disabling neurological disease in young adults. Relapsing remitting MS (RRMS) is the most common form of MS, and around 85% of people with MS are diagnosed with this type.[3] The exact cause of MS is unknown but it is thought that the body's immune system attacks myelin, disrupting the information flow along the nerves. There is currently no cure for MS, but treatments are available to help slow the course of the disease.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 billion in 66 countries. Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany, holds the global rights to the „*Merck KGaA, Darmstadt, Germany*" name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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[1] MS Society of Canada. What is MS. Accessed April 24, 2017. Available at: https://mssociety.ca/about-ms/what-is-ms
[2] MAVENCLAD™ Product Monograph. November 2017