

## News Release

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### **FDA Accepts File for Cladribine Tablets as Potential Treatment for Relapsing Forms of Multiple Sclerosis**

- **Cladribine tablets is an investigational oral therapy with proposed dosing of a maximum of 20 days over two years with no additional dosing required in years 3 and 4**
- **The New Drug Application includes close to 12,000 patient years of data and up to 10 years of safety data in some patients**
- **Cladribine tablets is approved as MAVENCLAD® in 38 countries**

Darmstadt, Germany, July 30, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, which operates its biopharmaceutical business as EMD Serono in the U.S. and Canada, today announced that a resubmission of the New Drug Application (NDA) for cladribine tablets as a potential treatment for patients with relapsing forms of multiple sclerosis (MS) has been accepted for filing by the U.S. Food and Drug Administration (FDA).

“We are delighted the FDA has accepted cladribine tablets for filing,” said Belén Garijo, Member of the Executive Board and CEO Healthcare of Merck KGaA, Darmstadt, Germany. “Our goal is to offer cladribine tablets to patients and physicians in the U.S. as a new treatment paradigm for relapsing MS, and we look forward to working closely with the FDA throughout the review process.”

The acceptance indicates that the FDA has found the company’s resubmission sufficiently complete to permit a substantive review. The resubmission is in response to the Complete Response Letter issued by the FDA in 2011 requesting an improved understanding of safety risks and the overall benefit-risk profile.

The NDA acceptance follows global approvals of cladribine tablets under the trade name Mavenclad® in 38 countries since August 2017, including the European



Union (EU), Canada, Australia, Israel, Argentina, United Arab Emirates, Chile and Lebanon. Additional filings in other countries are planned for 2018.

Cladribine tablets is an investigational agent that has been studied as a short-course (a maximum of 20 days of treatment over two years) oral therapy that is thought to selectively target lymphocytes, which may be integral to the pathological process of relapsing MS.

“Most available MS therapies require continued, regular dosing of medication. A treatment approach consisting of short, infrequent oral treatment cycles may help lower the treatment burden for patients,” said Thomas Leist, M.D., PhD, Director, Comprehensive Multiple Sclerosis Center at Jefferson University Hospitals, Philadelphia, USA. “Based on additional clinical research in recent years, we know more about the treatment course, safety, and impact of cladribine tablets across several key measures of MS, and hope it will be made available to the U.S. MS community.”

The NDA acceptance includes close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of safety data in some patients. The clinical development program included data from three Phase III trials, CLARITY, CLARITY EXT and ORACLE MS, the Phase II ONWARD study and long-term follow-up data from the eight-year prospective registry, PREMIERE.

### **Cladribine Tablets**

Cladribine tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received approvals for patients with highly active RMS as defined by clinical or imaging features in the European Union (EU), Israel, Argentina, United Arab Emirates, Chile and Lebanon. In December 2017, Health Canada and the Therapeutic Goods Administration (TGA) in Australia approved MAVENCLAD® for the treatment of relapsing-remitting MS (RRMS).

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 Phase III placebo-controlled study following on from the CLARITY study, which evaluated the safety and efficacy of cladribine tablets over two additional years beyond the two-year CLARITY study, according to the treatment assignment scheme for years 3 and 4.
- 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

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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) study: a long-term follow-up safety registry of multiple sclerosis patients who participated in cladribine tablets clinical studies.

The clinical development program of cladribine tablets in MS comprises close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of follow-up in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with cladribine tablets was lymphopenia. The incidence of infections was 48.3% with cladribine tablets and 42.5% with placebo, with 99.1% and 99.0% respectively rated mild-to-moderate by investigators.

### Multiple Sclerosis

Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that approximately 2.3 million people have MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

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### Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of €15.3 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“ name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.