

## NEWS RELEASE

# EMD Serono Presents New MAVENCLAD® (Cladribine) Tablets Data Highlighting Sustained Reduction in NfLs and Benefit of Early Initiation

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- New data showed sustained reduction in neurofilament light chain (NfL) levels over two years of treatment with MAVENCLAD® (cladribine) tablets in patients with relapsing multiple sclerosis (RMS)
- Findings from real-world evidence (RWE) studies suggest a shift toward the use of cladribine tablets in treatment-naïve RMS patients with high rates of treatment continuation at four years

ROCKLAND, Mass.--(BUSINESS WIRE)-- EMD Serono, the Healthcare business sector of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced the presentation of new analyses from the MAVENCLAD® (cladribine) tablets MAGNIFY-MS study, which demonstrated that patients with relapsing multiple sclerosis (RMS) experienced sustained reduction in serum neurofilament light chain (NfL), indicating that MAVENCLAD reduced neuronal injury over two years. Additional data include two real-world evidence (RWE) studies, which indicated an increase in the use of cladribine tablets in treatment-naïve patients and demonstrated low levels of switching to other disease-modifying therapies (DMTs) up to four years. These data were presented at the 9th Joint ECTRIMS- ACTRIMS meeting in Milan, Italy.

Analyses from the post-hoc MAGNIFY-MS study showed that throughout the two-year treatment course of MAVENCLAD, median serum NfL Z-scores were reduced in all patient groups compared to baseline. These findings suggest that MAVENCLAD effectively reduced neuronal injury across magnetic resonance imaging (MRI) outcome subgroups.

"Our commitment to the MS community drives our unwavering focus on generating data that provide further insights into the efficacy and safety of MAVENCLAD," said Alexander Kulla, Senior Vice President & Medical Unit

Head Neurology & Immunology at Merck KGaA, Darmstadt, Germany. "We know that serum NfL levels are increasingly used as an important biomarker in MS, signaling possible disease activity that can lead to progression. The findings presented at ECTRIMS-ACTRIMS demonstrate that MAVENCLAD produced sustained reductions in serum NfL without continuous immunosuppression."

Two real-world studies also presented at ECTRIMS-ACTRIMS reinforce the potential benefits of initiating treatment with cladribine tablets in the earlier stages of the disease. In the five-year follow-up of the CLARENCE study, conducted in the United Kingdom, it was found that 36.1% of 2,685 assessed patients were treatment-naïve during treatment commencement. In a separate study out of Latin America, data was analyzed from 1,421 patients who received at least one course of cladribine tablets. Over time, an increasing trend in treatment initiation among treatment-naïve patients was observed, suggesting an advantage of early utilization of cladribine treatment. As well in both studies, very few patients receiving cladribine tablets switched to other therapies.

## About MAVENCLAD®

MAVENCLAD, approved by the U.S. Food and Drug Administration (FDA) on March 29, 2019, is the first and only short-course oral therapy for the treatment of adults with relapsing-remitting disease (RRMS) and active secondary progressive disease (SPMS). Because of its safety profile, use of MAVENCLAD is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of multiple sclerosis (MS), and MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS). Patients should follow healthcare provider instructions including cancer screening, contraception and blood tests. The approved dose of MAVENCLAD is 3.5 mg per kg body weight over two years, administered as one treatment course of 1.75 mg per kg per year, each consisting of two treatment weeks. The mechanism by which cladribine exerts its therapeutic effects in patients with multiple sclerosis has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. MAVENCLAD causes a dose-dependent reduction in lymphocyte counts followed by recovery.

Because cladribine is cytotoxic, special handling and disposal instructions should be followed.

MAVENCLAD has been approved in over 80 countries, including the European Union (EU), Canada, Australia and Switzerland, for various relapsing MS indications. Visit [www.MAVENCLAD.com](http://www.MAVENCLAD.com) for more information.

## IMPORTANT SAFETY INFORMATION

### WARNING: MALIGNANCIES and RISK OF TERATOGENICITY

- Treatment with MAVENCLAD may increase the risk of malignancy. MAVENCLAD is contraindicated in patients

with current malignancy. In patients with prior malignancy or with increased risk of malignancy, evaluate the benefits and risks of the use of MAVENCLAD on an individual patient basis. Follow standard cancer screening guidelines in patients treated with MAVENCLAD

- MAVENCLAD is contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the potential for fetal harm. Malformations and embryolethality occurred in animals. Exclude pregnancy before the start of treatment with MAVENCLAD in females of reproductive potential. Advise females and males of reproductive potential to use effective contraception during MAVENCLAD dosing and for 6 months after the last dose in each treatment course. Stop MAVENCLAD if the patient becomes pregnant

## CONTRAINDICATIONS

- Patients with current malignancy.
- Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during and for 6 months after the last dose in each treatment course. May cause fetal harm.
- Patients with human immunodeficiency virus (HIV).
- Patients with active chronic infections (e.g., hepatitis or tuberculosis).
- Patients with a history of hypersensitivity to cladribine.
- Women intending to breastfeed while taking MAVENCLAD tablets and for 10 days after the last dose.

## WARNINGS AND PRECAUTIONS

- Malignancies: Treatment with MAVENCLAD may increase the risk of malignancy. After the completion of 2 treatment courses, do not administer additional MAVENCLAD treatment during the next 2 years. In clinical studies, patients who received additional MAVENCLAD treatment within 2 years after the first 2 treatment courses had an increased incidence of malignancy. The risk of malignancy with reinitiating MAVENCLAD more than 2 years after the completion of 2 treatment courses has not been studied. Follow standard cancer screening guidelines in patients treated with MAVENCLAD.
- Risk of Teratogenicity: MAVENCLAD may cause fetal harm when administered to pregnant women. In females of reproductive potential, exclude pregnancy before initiation of each treatment course of MAVENCLAD and prevent by the use of effective contraception during MAVENCLAD dosing and for at least 6 months after the last dose of each treatment course. Women who become pregnant during treatment with MAVENCLAD should discontinue treatment.
- Lymphopenia: MAVENCLAD causes a dose-dependent reduction in lymphocyte count. In clinical studies, 87% of MAVENCLAD-treated patients experienced lymphopenia. The lowest absolute lymphocyte counts occurred approximately 2 to 3 months after the start of each treatment course and were lower with each additional treatment course. Concomitant use of MAVENCLAD with hematotoxic drugs may increase the risk of adverse

reactions because of the additive hematological effects. Monitor lymphocyte counts before and during treatment, periodically thereafter, and when clinically indicated.

- **Infections:** MAVENCLAD can reduce the body's immune defense and may increase the likelihood of infections. Infections occurred in 49% of MAVENCLAD-treated patients compared to 44% of patients treated with placebo in clinical studies. The most frequent serious infections included herpes zoster and pyelonephritis. Single fatal cases of tuberculosis and fulminant hepatitis B were reported in the clinical program. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting MAVENCLAD. Screen patients for latent infections; consider delaying treatment until infection is fully controlled. Vaccinate patients antibody-negative to varicella zoster virus prior to treatment. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections. In patients treated with parenteral cladribine for oncologic indications, cases of progressive multifocal leukoencephalopathy (PML) have been reported. No case of PML has been reported in clinical studies of cladribine in patients with MS.
- **Hematologic Toxicity:** In addition to lymphopenia, decreases in other blood cells and hematological parameters have been reported with MAVENCLAD in clinical studies. In general, mild to moderate decreases in neutrophil counts, hemoglobin levels, and platelet counts were observed. Severe decreases in neutrophil counts were observed in 3.6% of MAVENCLAD-treated patients, compared to 2.8% of placebo patients. Obtain complete blood count (CBC) with differential including lymphocyte count before and during treatment, periodically thereafter, and when clinically indicated.
- **Risk of Graft-versus-Host Disease With Blood Transfusions:** Transfusion-associated graft-versus-host disease has been observed rarely after transfusion of nonirradiated blood in patients treated with cladribine for non-MS treatment indications.
- **Liver Injury:** In clinical studies, 0.3% of MAVENCLAD-treated patients had liver injury (serious or causing treatment discontinuation) compared to 0 placebo patients. Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment. Discontinue if clinically significant injury is suspected.
- **Hypersensitivity:** In clinical studies, 11% of MAVENCLAD-treated patients had hypersensitivity reactions, compared to 7% of placebo patients. Hypersensitivity reactions that were serious and/or led to discontinuation of MAVENCLAD, occurred in 0.5% of MAVENCLAD-treated patients, compared to 0.1% of placebo patients. If a hypersensitivity reaction is suspected, discontinue MAVENCLAD therapy. Do not use MAVENCLAD in patients with a history of hypersensitivity to cladribine.
- **Cardiac Failure:** In clinical studies, one MAVENCLAD-treated patient experienced life-threatening acute cardiac failure with myocarditis, which improved after approximately one week. Cases of cardiac failure have also been reported with parenteral cladribine used for treatment indications other than multiple sclerosis.

**Adverse Reactions:** The most common adverse reactions with an incidence of >20% for MAVENCLAD are upper respiratory tract infection, headache, and lymphopenia.

**Drug Interactions/Concomitant Medication:** Concomitant use of MAVENCLAD with immunosuppressive or myelosuppressive drugs and some immunomodulatory drugs (e.g., interferon beta) is not recommended and may increase the risk of adverse reactions. Acute short-term therapy with corticosteroids can be administered.

Avoid concomitant use of certain antiviral and antiretroviral drugs. Avoid concomitant use of BCRP or ENT/CNT inhibitors as they may alter bioavailability of MAVENCLAD.

**Use in Specific Populations:** Studies have not been performed in pediatric or elderly patients, pregnant or breastfeeding women. Use in patients with moderate to severe renal or hepatic impairment is not recommended.

Please see the full **Prescribing Information**, including **boxed WARNING** for additional information.

### About 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 2.8 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.

### EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science.

### About EMD Serono, Inc.

EMD Serono - the healthcare business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada - aspires to create, improve and prolong life for people living with difficult-to-treat conditions like infertility, multiple sclerosis and cancer. The business is imagining the future of healthcare by working to translate the discovery of molecules into potentially meaningful outcomes for people with serious unmet medical needs. EMD Serono's global roots go back more than 350 years with Merck KGaA, Darmstadt, Germany. Today, the business has approximately 1,500 employees around the country with commercial, clinical and research operations in Massachusetts.

[www.emdserono.com](http://www.emdserono.com).

### About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science,

healthcare and electronics. Around 60,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From providing products and services that accelerate drug development and manufacturing as well as discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2021, Merck KGaA, Darmstadt, Germany, generated sales of € 19.7 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

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