News Release

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New Data Presented at ACTRIMS Forum 2021 Indicate MAVENCLAD®-treated RMS Patients Mount Protective Antibody Response to Common Vaccines

- **MAGNIFY-MS retrospective analysis demonstrates patients develop protective antibody levels for at least six months following seasonal influenza and varicella zoster vaccines, irrespective of vaccine timing relative to MAVENCLAD dosing**
- **Initial findings from the CLOCK-MS vaccine sub-study show protective influenza antibody levels at four weeks post-vaccination in MS patients taking MAVENCLAD**
- **In both studies, protective antibody levels were maintained or increased independent of lymphocyte counts**

Darmstadt, Germany, February 25, 2021 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced the presentation of a new analysis from the MAGNIFY-MS study on MAVENCLAD® (cladribine) tablets in patients with relapsing multiple sclerosis (RMS) at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2021, being held virtually February 25-27, 2021. The data indicate that RMS patients receiving MAVENCLAD are able to mount a response to seasonal influenza and varicella zoster vaccination.

"Understanding vaccine efficacy in MS patients is particularly important in the face of the current pandemic and the growing availability of COVID-19 vaccines," said Klaus Schmierer, Professor of Neurology at Queen Mary University of London and The Royal London Hospital, UK. "Whilst this new information is based on a small

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News Release

cohort of patients receiving influenza and varicella zoster vaccines, it provides physicians with preliminary evidence that patients taking MAVENCLAD are able to mount and maintain effective vaccine responses."

In the U.S., the MAVENCLAD label states that all immunizations should be administered according to immunization guidelines prior to starting MAVENCLAD. The retrospective analysis was conducted to evaluate the protective antibody response to seasonal influenza (n=12) and varicella zoster virus (VZV) vaccination (n=3) in patients treated with MAVENCLAD. Blood samples taken before and after vaccination were examined. In patients who received the seasonal influenza vaccine, protective antibody levels were maintained or increased for at least six months independent of lymphocyte counts measured at the time of vaccination in year 1 or 2 of MAVENCLAD treatment. In patients who received the VZV vaccine before year 1 initiation of MAVENCLAD, protective VZV antibody levels were maintained over six months post-initiation with MAVENCLAD, despite lymphocyte depletion. These results were consistent irrespective of when the patients received the vaccine relative to their MAVENCLAD treatment.

In the CLOCK-MS vaccine sub-study analysis, three relapsing remitting multiple sclerosis (RRMS) patients had received at least one dose of MAVENCLAD prior to receiving an influenza vaccine. Protective antibody levels were increased at four weeks post-vaccination in all three patients. Two of these patients, who had received treatment with MAVENCLAD two and four months prior to vaccination, were experiencing lymphopenia around the time of vaccination.

"In an ever changing world where a pandemic will likely be present for the foreseeable future, it is critical to assess the impact of common non-live vaccinations in those taking disease modifying therapies," said Maria Rivas, MD, Chief Medical Officer, Healthcare business of Merck KGaA, Darmstadt, Germany. "We are committed to communicating timely real-world evaluations of our therapies to help answer relevant questions raised by the MS community."

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 for more information.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: MALIGNANCIES and RISK OF TERATOGENICITY

- **Treatment with MAVENCLAD may increase the risk of malignancy. MAVENCLAD is contraindicated in patients with current malignancy; evaluate the benefits and risks of the use of MAVENCLAD on an individual patient basis for patients with prior or increased risk of malignancy.**
- **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.**

CONTRAINDICATIONS

- Current malignancy.
- Pregnancy, and women and men of reproductive potential who do not plan to use effective contraception during MAVENCLAD dosing and for 6 m after the last dose in each treatment course.
- Human immunodeficiency virus (HIV).
- Active chronic infections (e.g., hepatitis or tuberculosis).
- History of hypersensitivity to cladribine.
- Breastfeeding while taking MAVENCLAD and for 10 days after the last dose.

DOSING CONSIDERATIONS: After the completion of 2 treatment courses, do not administer additional MAVENCLAD during the next 2 years. The risk of malignancy with reinitiating MAVENCLAD more than 2 years after completion of 2 treatment courses has not been studied.

ADDITIONAL WARNINGS AND PRECAUTIONS

- **Lymphopenia:** In clinical studies, 87% of MAVENCLAD-treated patients experienced lymphopenia. 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:** 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. Monitor for infections. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. 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**: 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

News Release

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**: Irradiation of cellular blood components is recommended.
- **Liver Injury**: Obtain liver function tests prior to treatment. Discontinue MAVENCLAD if significant injury is suspected.
- **Hypersensitivity**: In clinical studies, 11% of MAVENCLAD-treated patients had hypersensitivity reactions, compared to 7% of placebo patients. Serious hypersensitivity reactions occurred in 0.5% of MAVENCLAD-treated patients, compared to 0.1% of placebo patients. If a hypersensitivity reaction is suspected, discontinue treatment. 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. 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.

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 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.

Merck KGaA, Darmstadt, Germany in Neurology and Immunology
Merck KGaA, Darmtadt, Germany has a long-standing legacy in neurology and immunology, with significant R&D and commercial experience in multiple sclerosis (MS). The company`s current MS portfolio includes two products for the treatment of relapsing MS – Rebif® (interferon beta-1a) and MAVENCLAD® (cladribine) tablets. Merck KGaA, Darmtadt, Germany aims to improve the lives of patients by addressing areas of unmet medical needs. In addition to the company`s commitment to MS, the company also have a pipeline focusing on discovering new therapies that have the potential in other neuroimmune diseases.

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 58,000 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 advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 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 EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 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.