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News Release

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June 18, 2018

Data Presented at EAN 2018 Provide Further Insight into the Efficacy of Investigational Cladribine Tablets in Patients with Relapsing Forms of Multiple Sclerosis (MS)

- **Post-hoc analysis of CLARITY study demonstrates clinical and Magnetic Resonance Imaging efficacy in subgroups of both younger and older adults treated with Cladribine Tablets**
- **Analysis with Multi-Criteria Decision Analysis (MCDA) methodology provided results comparing EU-approved Cladribine Tablets with other approved treatments in patients with highly active MS**

Darmstadt, Germany, June 18, 2018 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the U.S. and Canada, today announced the presentation of new efficacy and benefit-risk assessment data for Cladribine Tablets at the 4th Congress of the European Academy of Neurology (EAN), in Lisbon, Portugal. Results of a retrospective analysis of the Phase III CLARITY study showed clinical and Magnetic Resonance Imaging (MRI) benefits in patients with relapsing remitting multiple sclerosis (RRMS) aged ≤50 and >50 years and treated with Cladribine Tablets, with improvements observed in both relapse rate and MRI outcomes when compared with placebo.

The aim of the post-hoc analysis of the Phase III CLARITY study was to investigate whether the clinical and MRI effects of Cladribine Tablets are consistent in both older and younger patients. The results highlight the improvements observed in annualized relapse rate (ARR) and MRI outcomes versus placebo in both subgroups of RRMS patients, ≤50 and >50 years; Cladribine Tablets reduced relapse risk compared to placebo by 59% and 52%, respectively. In placebo treated patients, there were higher mean numbers of new T1 Gd+ and active T2 lesions for those aged ≤50 years compared to patients aged >50. Despite this, treatment with

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Cladribine Tablets demonstrated significant effects on MRI measures in both age groups (P<0.0001).

Additional data presented at EAN 2018 provide the results of the EMA-recommended application of Multi-Criteria Decision Analysis (MCDA) methodology to assess the benefit-risk profile of Cladribine Tablets, which is approved in Europe for the treatment of highly active relapsing forms of multiple sclerosis as defined by clinical or imaging features, to assess the benefit-risk profile of Cladribine Tablets preferences among five blinded treating neurologists in Europe, versus other approved DMDs*, in MS patients with high disease activity. Results of this analysis suggest a comparable benefit-risk profile for Cladribine Tablets in patients with high disease activity when compared to that of five other DMDs, in this assessment.

"The presentation of these data highlight our ongoing commitment to understanding the full benefit-risk profile of Cladribine Tablets in a broad range of patients. Post hoc data from the CLARITY study, coupled with results from a Multi-Criteria Decision Analysis, which are based on expert physician assessment and practice-relevant treatment considerations, form a potentially useful tool for physicians in countries where Cladribine Tablets is approved to evaluate therapy options for patients with high disease activity," said Luciano Rossetti, Head of Global R&D for the biopharma business of Merck KGaA, Darmstadt, Germany. "The MCDA methodology is one that is recommended by EMA, and we are pleased that Cladribine Tablets performed well using this approach."

Furthermore, additional post-hoc data from clinical studies of patients treated with Rebif (interferon beta-1a) showed that the MAGNIMS score at Year 1 reliably predicted long-term clinical disease activity (CDA)-free status and disability progression. At Year 1 the median time to a CDA event was longer in patients with a MAGNIMS score of 0, versus those with score 1 or 2. Additionally, median time to Expanded Disability Status Scale (EDSS) progression was found to be longer in patients with a Year 1 MAGNIMS score of 0 (7.5 years), versus those with a score of 1 (4.0 years) or 2 (2.5 years).

* Approved DMDs available in European Union countries at the time of assessment (December 2015): alemtuzumab, dimethyl fumarate, fingolimod, natalizumab, and teriflunomide

Additionally, a presentation from the Merck KGaA, Darmstadt, Germany-sponsored MS in the 21st Century joint patient-physician steering group highlighted the results of an international unmet needs survey, suggesting a disconnect between patients' and physicians' perspectives of MS treatment decisions. The results of this survey indicate that MS patients have different perceptions of the current unmet needs in the disease area compared to healthcare professionals (HCPs). Whilst 87.7% of HCPs considered that they involved their patients in the decision-making process, only 38.9% of patients reported they felt involved. Addressing this disconnect between patients' and physicians' perspectives during treatment discussions could lead to an improved dialogue between HCPs and patients, an integral step towards finding appropriate individualised treatment approaches for each patient.

About 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 marketing authorization in 35 countries including European Union member countries, Canada, Australia, Argentina, Israel, and the United Arab Emirates. MAVENCLAD® is now available in Germany, UK, Canada, Netherlands, Norway, Denmark, Sweden, Israel, and other markets.

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.

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 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.

About Rebif® (interferon beta-1a)
Rebif (interferon beta-1a) is used to treat relapsing forms of MS to decrease the frequency of relapses and delay the occurrence of some of the physical disability that is common in people with MS. The efficacy and safety of Rebif in controlled clinical trials beyond 2-years has not been established.

Important Safety Information:
Rebif is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation.

Rebif should be used with caution in patients with depression, a condition that is common in people with multiple sclerosis. Depression, suicidal ideation, and suicide attempts have been reported to occur with increased frequency in patients receiving interferon compounds, including Rebif.

Severe liver injury, including some cases of hepatic failure requiring liver transplantation, has been reported rarely in patients taking Rebif. The potential for liver injury should be considered when used in combination with other products associated with liver injury. Monitor liver function tests and patients for signs and symptoms of hepatic injury. Consider discontinuing Rebif if hepatic injury occurs.

Anaphylaxis and other allergic reactions (some severe) have been reported as a rare complication of Rebif. Discontinue Rebif if anaphylaxis occurs.

In controlled clinical trials, injection site reactions occurred more frequently in Rebif-treated patients than in placebo-treated and Avonex-treated patients. Injection site reactions including injection site pain, erythema, edema, cellulitis, abscess, and necrosis have been reported in the postmarketing setting. Do not administer Rebif into affected area until fully healed; if multiple lesions occur, discontinue Rebif until skin lesions are healed.

Decreased peripheral blood counts in all cell lines, including pancytopenia, have been reported in Rebif-treated patients. In controlled clinical trials, leukopenia occurred at a higher frequency in Rebif-treated patients than in placebo and Avonex-treated patients. Thrombocytopenia and anemia occurred more frequently in 44 mcg Rebif-treated patients than in placebo-treated patients. Patients should be monitored for symptoms or signs of decreased blood counts. Monitoring of complete blood and differential white blood cell counts is also recommended.

Cases of thrombotic microangiopathy (TMA), some fatal, have been reported with interferon beta products, including Rebif, up to several weeks or years after starting therapy. Discontinue Rebif if clinical symptoms and laboratory findings consistent with TMA occur, and manage as clinically indicated.

Caution should be exercised when administering Rebif to patients with pre-existing seizure disorders. Seizures have been temporally associated with the use of beta interferons, including Rebif, in clinical trials and in postmarketing reports.

The most common side effects with Rebif are injection-site disorders, headaches, influenza-like symptoms, abdominal pain, depression, elevated liver enzymes, and hematologic abnormalities.

There are no adequate and well-controlled studies in pregnant women. Rebif should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Rebif full prescribing information is available
at http://www.emdserono.com/ms.country.us/en/images/Rebif_PI_tcm115_140051.pdf?Version=

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 2.3 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.

About 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.