News Release

Your Contact
Gangolf Schrimpf +49 6151 72-9591
Investor Relations +49 6151 72-3321

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Cladribine Tablets Receives Positive CHMP Opinion for Treatment of Relapsing Forms of Multiple Sclerosis

- **Efficacy and safety data support positive benefit / risk assessment from CHMP**
- **Cladribine Tablets is the first and only investigational medicinal product to have shown a sustained 4 years of disease control with a maximum of 20 days of oral treatment over 2 years in clinical trials**

Darmstadt, Germany, June 23, 2017 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion for approval of Cladribine Tablets (proposed tradename MAVENCLAD™) for the treatment of relapsing forms of multiple sclerosis (RMS) in patients with high disease activity.

“The positive opinion from the CHMP is an extraordinary development for our company, affirming our belief in Cladribine Tablets as a potential important treatment option for patients living with multiple sclerosis,” said Belén Garijo, member of the Executive Board of Merck KGaA, Darmstadt, Germany, and CEO Healthcare. “We now eagerly await the European Commission decision, and the opportunity to make a difference in the MS treatment paradigm. Our sincerest thanks to the entire MS community for their unwavering support throughout the Cladribine Tablets journey.”

“We strongly believe in the therapeutic value of Cladribine Tablets and the significant impact this investigational therapy may have on the future of MS care,” said Luciano Rossetti, Global Head of R&D for the biopharma business of Merck KGaA, Darmstadt,

Frankfurter Strasse 250
64293 Darmstadt · Germany
Hotline +49 6151 72-5000
www.emdgroup.com

Head Media Relations -62445
Spokesperson: -9591 / -7144 / -6328
Fax +49 6151 72 3138
media.relations@emdgroup.com

Germany. “There are still significant unmet needs for patients with MS, particularly those with high disease activity. We look forward to our continued partnership with the EMA, which has been an invaluable scientific advisor in helping us advance the development of Cladribine Tablets.”

The CHMP positive opinion is based on 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. The clinical development program included data from three Phase III trials, CLARITY, CLARITY EXTENSION and ORACLE MS, the Phase II ONWARD study and long-term follow-up data from the 8-year prospective registry, PREMIERE. The efficacy and safety results of these studies allowed a full characterization of the benefit-to-risk profile of Cladribine Tablets.

In patients with high disease activity, post hoc analyses of the two-year Phase III CLARITY trial demonstrated that Cladribine Tablets reduced the annualised relapse rate by 67% and the risk of 6-month confirmed EDSS progression by 82% versus placebo. As demonstrated in the Phase III CLARITY EXTENSION study no further Cladribine treatment was required in Years 3 and 4. The comprehensive dataset has informed the posology and monitoring requirements. The most important side effects are lymphopenia, which can be severe and long-lasting, and infections, including herpes zoster.

The CHMP’s recommendation will be referred to the European Commission which is expected to make a final decision on the marketing authorisation application for Cladribine Tablets within 67 days from the CHMP opinion.

MAVENCLAD™ is the proprietary name submitted to EMA for the investigational medicine Cladribine Tablets.

About MAVENCLAD™
MAVENCLAD™ (cladribine tablets) is an investigational short-course oral therapy that selectively and periodically targets lymphocytes thought to be integral to the pathological process of MS. MAVENCLAD is currently under clinical investigation and not yet approved for the treatment for any use in the United States, Canada and Europe. In July 2016, the European Medicines Agency (EMA) accepted for review the Marketing Authorisation Application (MAA) of MAVENCLAD™ for the treatment of relapsing remitting multiple sclerosis.

The clinical development program for MAVENCLAD includes:

- The CLARITY (CLAdRIbine Tablets Treating MS OralIY) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of MAVENCLAD as a monotherapy in patients with RRMS.
- The CLARITY extension study: a four-year Phase III placebo-controlled study following on from the CLARITY study, designed to evaluate the safety and efficacy of MAVENCLAD 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 MAVENCLAD 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 MAVENCLAD 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 MAVENCLAD. The follow-up will consist of over 10,000 patient years of exposure in total, with follow-up in some patients exceeding eight years at completion.

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. 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" name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.