Merck KGaA
Darmstadt, Germany

News Release

Your Contact

Erin-Marie Beals +1 781-681-2850

September 16, 2016

Merck KGaA, Darmstadt, Germany, Presents New Data Examining Durable Efficacy with Investigational Cladribine Tablets in Multiple Sclerosis

- **Phase III studies highlight lasting reductions in relapse rates for an additional two years following short oral treatment courses in year one & year two with Cladribine Tablets**

Darmstadt, Germany, September 16, 2016 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, announced they presented new efficacy data for investigational Cladribine Tablets in two oral presentations at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) taking place September 14-17, 2016, in London. The findings, from the phase III CLARITY and CLARITY EXTENSION trials and from the open-label maintenance period of the phase III ORACLE-MS study, demonstrated durable efficacy of Cladribine Tablets in patients with multiple sclerosis (MS) along with a well-characterized safety profile. CLARITY and CLARITY EXTENSION studies confirmed that 20 days of oral dosing over two years was effective in reducing the frequency of relapses and slowing disability progression for up to four years.

"The results presented this week show that the clinical benefits of Cladribine Tablets can be maintained in most patients for an additional two years without the need for redosing," said Dr. Giancarlo Comi, Professor of Neurology, Chairman of the Department of Neurology, and Director of the Institute of Experimental Neurology, at Vita-Salute San Raffaele University, Scientific Institute San Raffaele, Milan and a lead investigator in the studies. "Although multiple therapies are

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

available for patients with MS, there is still a large unmet need within this patient community, including for therapies that offer lasting benefits."

In one oral presentation, data from the two-year phase III CLARITY trial and its two-year extension study (CLARITY EXTENSION) showed that patients with relapsing MS who received placebo in CLARITY and were switched to Cladribine Tablets in CLARITY EXTENSION had significantly reduced annualised relapse rates (ARR) (0.26 vs. 0.10, P<0.0001) and were significantly more likely to be relapse free (58.0 percent vs. 79.6 percent, P<0.0001) at the end of the extension phase. ARR were maintained for patients who received Cladribine Tablets for two years in CLARITY and were then switched to placebo for two years in the extension phase.

The second oral presentation reported data from the open-label maintenance period of the phase III ORACLE-MS study. ORACLE-MS showed that, for patients with a first demyelinating event, treatment with Cladribine Tablets significantly reduced the risk of progression to clinically definite MS compared with placebo. For the open-label portion of the study, patients who converted to clinically definite MS during the initial treatment period were switched to Rebif® therapy. The new data presented at ECTRIMS show that patients who had received Cladribine Tablets in the initial treatment phase had lower ARR over the maintenance period (median time on Rebif = 56.0 weeks) compared with those who had received placebo in the initial treatment phase [0.14 for Cladribine Tablets 3.5 mg/kg (n=25), 0.24 for Cladribine Tablets 5.25 mg/kg (n=24) and 0.42 for placebo (n=60)].

"Cladribine Tablets has a unique oral dosing schedule, with just two short treatment courses administered orally in years one and two. Together with more than 10,000 patient years of safety data and phase III efficacy data, these findings of lasting reductions in relapse rates support our belief that, if approved, Cladribine Tablets may serve as an important new advance for patients with relapsing-remitting MS," said Luciano Rossetti, Head of Global R&D for the Biopharma business of Merck KGaA, Darmstadt, Germany.

The European Medicines Agency (EMA) has accepted for review the Marketing Authorization Application (MAA) of the investigational product Cladribine Tablets for the treatment of relapsing-remitting MS.

About Cladribine Tablets
Cladribine Tablets is an oral small molecule prodrug that selectively and periodically targets lymphocytes thought to be integral to the pathological process of MS. Cladribine Tablets is currently under clinical investigation and not approved for any use in the United States, Canada and Europe.

About Rebif®
Rebif® (interferon beta-1a) is a disease-modifying drug used to treat relapsing forms of multiple sclerosis (MS) and is similar to the interferon beta protein produced by the human body. The efficacy of Rebif® in chronic progressive MS has not been established. Interferon ß is thought to help reduce inflammation. The exact mechanism is unknown.

Rebif®, which was approved in Europe in 1998 and in the US in 2002, is registered in more than 90 countries worldwide. Rebif® has been proven to delay the progression of disability, reduce the frequency of relapses and reduce MRI lesion activity and area*.

Rebif® can be administrated with the RebiSmart® electronic auto-injection device (not approved in the US), or with the RebiDose® single-use disposable pen, or the manual multidose injection pen RebiSlide™. Rebif® can also be administered with the autoinjector Rebiject II® or by manual injection using ready-to-use pre-filled syringes. These injection devices are not approved in all countries.

In January 2012, the European commission approved the extension of the indication of Rebif® in early multiple sclerosis. The extension of the indication of Rebif® has not been submitted in the United States.

Rebif® should be used with caution in patients with a history of depression, liver disease, thyroid abnormalities and seizures. Most commonly reported side effects are flu-like symptoms, injection site disorders, elevation of liver enzymes and blood cell abnormalities. Patients, especially those with depression, seizure disorders, or liver problems, should discuss treatment with Rebif® with their doctors.

*The exact correlation between MRI findings and the current or future clinical status of patients, including disability progression, is unknown.

Rebif® (interferon beta-1a) is approved in the United States for relapsing forms of MS. RebiSmart®, an electronic device for self-injection of Rebif®, is also not approved in the United States. Cladribine Tablets is an investigational product and not approved for use in any indication in the United States.

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.

All Merck KGaA, Darmstadt, Germany, press releases are distributed by e-mail at the same time they become available on the EMD Group Website. In case you are a resident of the USA or Canada please go to www.emdgroup.com/subscribe to register again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

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 2015, Merck KGaA, Darmstadt, Germany, generated sales of € 12.85 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 KGaA, Darmstadt, Germany, name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.