News Release

Your Contact
Erin-Marie Beals +1 781-681-2850

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Data on Investigational Cladribine Tablets and Rebif® (interferon beta-1a) in Relapsing Forms of Multiple Sclerosis (MS) to be Presented at EAN 2018

- **14 abstracts to be presented, further characterizing the profiles of Cladribine Tablets and Rebif (interferon beta-1a)**

Darmstadt, Germany, June 14, 2018 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the U.S. and Canada, will present data from its neurology and immunology portfolio at the 4th Congress of the European Academy of Neurology (EAN), taking place from June 16-19, in Lisbon, Portugal. The Company will present a total of 14 abstracts in the area of relapsing multiple sclerosis (RMS), including a post-hoc analysis of the Phase III CLARITY study, investigating whether the clinical and magnetic resonance imaging (MRI) effects of Cladribine Tablets are consistent in older (>50 years) and younger (≤50) patients with relapsing remitting MS (RRMS). Data presented at the congress will also provide further insights into the benefit-risk profile of Cladribine Tablets in patients with relapsing forms of MS with high disease activity, using Multi-Criteria Decision Analysis, an EMA-recommended methodology to compare the benefit-risk profile between treatments. A separate post-hoc analysis of patients in the ONWARD study evaluates the efficacy of Cladribine Tablets as add-on to interferon beta-1a in patients with secondary progressive MS (SPMS) with relapses, compared to patients with RRMS from the same study.

Additionally, data presentations on Rebif® (interferon beta-1a) include analysis of MRI in MS (MAGNIMS) score* to predict long-term clinical disease activity (CDA)-free status and disability progression following treatment with Rebif®.

* Magnetic Resonance Imaging in MS

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

In line with the Company's MS Inside Out campaign aiming to better understand patients with MS, results of the Merck KGaA, Darmstadt, Germany-sponsored 'MS in the 21st Century International Unmet Needs Survey' show that MS patients have substantially different perceptions of the current unmet needs in MS compared to healthcare professionals (HCPs). Identification and understanding of these differences could lead to an improved dialogue between HCPs and patients, which is integral to finding appropriate individualised treatment approaches for each patient.

Attendees can learn more about the Company's programs, pipeline and activities in neurology and immunology by visiting our medical booth medical booth A07.

The following abstracts have been accepted for presentation at EAN Congress 2018:

Cladribine Tablets Presentations			
Title	**Authors**	**Abstract No.**	**Presentation Date/Time/Session**
Infections during periods of grade 3 or 4 lymphopenia in patients taking cladribine tablets 3.5 mg/kg: data from an integrated safety analysis	Cook S, Leist T, Comi G, Montalban X, Sylvester E, Hicking C, Dangond F	748	ePoster 16-18 Jun 2018 Time:12:30-14:15
Effects of cladribine tablets on CD4+ T cell subsets in the ORACLE-MS study: Results from an analysis of lymphocyte surface markers	Stuve O, Soelberg-Sorensen P, Leist T, Hyvert Y, Damian D, Boschert U	762	ePoster 16-18 Jun 2018 Time:12:30-14:15
Innate Immune Cell Counts in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS) Treated with Cladribine Tablets 3.5 mg/kg in CLARITY and CLARITY Extension	Soelberg-Sorensen P, Dangond F, Hicking C, Giovannoni G	749	ePresentation 16-18 Jun 2018 Time:12:30-14:15

Cladribine tablets produce selective and discontinuous reduction of B and T lymphocytes and natural killer cells in patients with early and relapsing multiple sclerosis (ORACLE-MS, CLARITY and CLARITY Extension)	Stuve O, Soelberg-Sorensen P, Giovannoni G, Leist T, Hyvert Y, Damian D, Boschert U	746	ePresentation 16-18 Jun 2018 Time:12:30-14:15
An analysis of malignancy risk in the clinical development programme of cladribine tablets in patients with relapsing multiple sclerosis (RMS)	Galazka A, Nolting A, Cook S, Leist T, Comi G, Montalban X, Hicking C, Dangond F	757	ePoster 16-18 Jun 2018 Time:12:30-14:15
Pregnancy outcomes during the clinical development programme of cladribine in multiple sclerosis (MS): an integrated analysis of safety for all exposed patients	Galazka A, Nolting A, Cook S, Leist T, Comi G, Montalban X, Hicking C, Dangond F	765	ePresentation 16-18 Jun 2018 Time:12:30-14:15
A benefit-risk assessment of cladribine tablets using Multi-Criteria Decision Analysis for patients with relapsing multiple sclerosis demonstrating high disease activity	Vermersch P, Martinelli V, Pfleger C, Rieckmann P, Galazka A, Dangond F, Phillips L	759	ePoster 16-18 Jun 2018 Time:12:30-14:15
Efficacy of cladribine tablets 3.5 mg/kg added to interferon-beta in patients with secondary progressive multiple sclerosis (SPMS) or relapsing-remitting multiple sclerosis (RRMS): a post-hoc analysis from ONWARD	Montalban X, Cohen B, Leist T, Moses H, Hicking C, Dangond F	766	ePresentation 16-18 Jun 2018 Time:12:30-14:15

A pooled analysis of the efficacy of cladribine tablets 3.5 mg/kg in patients with EDSS ≥3.5 or ≤3.0 at baseline in the CLARITY and ONWARD studies	Giovannoni G, Montalban X, Hicking C, Dangond F	747	ePresentation 16-18 Jun 2018 Time:12:30-14:15
Efficacy of cladribine tablets 3.5 mg/kg in patients with highly active relapsing multiple sclerosis (RMS): Pooled analysis of the double-blind cohort from CLARITY and ONWARD	Giovannoni G, Montalban X, Damian D, Dangond F	1345	ePresentation 16-18 Jun 2018 Time:12:30-14:15
Efficacy of cladribine tablets 3.5 mg/kg in patients ≤50 and >50 years of age with relapsing-remitting multiple sclerosis (RRMS): a post hoc analysis from CLARITY	Giovannoni G, Rammohan K, Cook S, Comi G, Rieckmann P, Soelberg-Sørensen P, Vermersch P, Dangond F, Damian D	1341	ePresentation 16-18 Jun 2018 Time:12:30-14:15
Rebif® (interferon beta-1a) Presentations			
Disease activity as assessed by the MAGNIMS score predicts long-term clinical disease activity free status and disability progression in patients treated with subcutaneous interferon beta-1a	Sormani MP, Freedman MS, Aldridge J, Marhardt K, De Stefano N	743	ePresentation 16-18 Jun 2018 Time:12:30-14:15
Evolution of new lesions and its temporal patterns in patients with clinically isolated syndrome treated with subcutaneous interferon beta-1a	Vrenken H, de Vos ML, Battaglini M, Nagtegaal GJ, de Almeida Teixeira BC, Marhardt K, De Stefano N, Barkhof F	444	ePresentation 16-18 Jun 2018 Time:12:30-14:15
Additional Company-sponsored Presentations			

Patient involvement in treatment decision-making: a sub-analysis of the 'MS in the 21st Century international unmet needs survey' comparing patient and healthcare professional perspectives	Rieckmann P, Langdon D on behalf of MS in the 21st Century Steering Group, and Contango EV	1340	Poster on Display

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. In December 2017, Health Canada approved MAVENCLAD® for the treatment of relapsing forms of MS.

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.