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News Release

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# Merck KGaA, Darmstadt, Germany's Phase IIb ADDRESS II Results Confirm Potential of Atacicept as a Candidate Therapy for SLE

- **Data presented at the 2016 American College of Rheumatology / Association of Rheumatology Health Professionals (ACR / ARHP) Annual Meeting (Abstract Number: 12L)**

Darmstadt, Germany, November 14, 2016 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced the results of the ADDRESS II Phase IIb, multicenter study on atacicept in patients with systemic lupus erythematosus (SLE).

Patients on standard-of-care therapy (n=306) were randomized to weekly subcutaneous injections of atacicept (75 or 150 mg) or placebo for 24 weeks. The primary endpoint was the proportion of patients achieving a clinical response as defined by a composite SLE Responder Index (SRI)-4 at week 24. Secondary endpoints included SRI-6 response rate and time to severe flare, assessed by SLEDAI flare index (SFI) or BILAG.

Although the primary endpoint was not met in the overall study population, there was a trend favoring atacicept with statistical significance achieved in a pre-specified sensitivity analysis of the primary endpoint using treatment Day 1 as baseline (rather than screening visit); atacicept 75 mg (55.9%, adjusted odds ratio/OR 1.88, p=0.029) and 150 mg (55.8%, adjusted OR 1.96, p=0.020) compared with placebo (41.0%). BILAG A flare was significantly reduced compared to placebo with atacicept 75 mg (p=0.019), and severe SFI flare reduced with 150 mg (p=0.002).



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Additionally, analyses of a predefined subpopulation of patients with high disease activity (HDA; SLEDAI-2K≥10, n=158) demonstrated statistically significant treatment effects of atacicept when compared to placebo. SRI-6 response at week 24 was significantly greater with atacicept 150 mg (54.9%, adjusted OR 3.30, p=0.005) compared with placebo (28.8%). Both atacicept doses led to significant reductions in the incidence of severe flare versus placebo, BILAG A flare (150 mg, hazard ratio/HR 0.32, p=0.038; 75 mg, HR 0.08, p=0.002) and SFI flare (150 mg, HR 0.19, p=0.004; 75 mg, HR 0.33, p=0.029).

“This is an impressive result, and particularly remarkable for having been achieved in a small study and in 24 weeks,” said Dr. Joan Merrill, Coordinating Investigator for the ADDRESS II study. ”If confirmed in future studies, this could hold exciting possibilities for our patients.”

Luciano Rossetti, Head of Global Research & Development for the biopharma business of Merck KGaA, Darmstadt, Germany added, “Building on the results of the APRIL SLE study, the results of ADDRESS II show that atacicept has the potential to become an important option for patients with lupus. We are particularly encouraged by the results in patients with high disease activity – which was approximately 50% of the patients in the ADDRESS II study. We are looking forward to discussions with the regulatory authorities.”

Atacicept was also associated with increased serum complement C3 and C4, and decreased IgG, IgM, IgA, and anti-dsDNA antibodies over time. Treatment-emergent adverse event incidence was slightly higher with atacicept (150 mg, 80.8%; 75 mg, 81.4%) than placebo (71.0%), however, the risks of serious adverse events or serious/severe infections were not increased with atacicept versus placebo, and there were no deaths. The safety findings were comparable for the high disease activity subpopulation, in that the risks of serious adverse events or serious/severe infections were not increased with atacicept versus placebo.

These results will be presented in a late-breaking poster session, “Efficacy and Safety of Atacicept in Patients with Systemic Lupus Erythematosus: Results of a 24-week Randomized, Placebo-Controlled, Phase IIb Study,”

at the 2016 American College of Rheumatology/Association of Rheumatology Health Professionals (ACR/ARHP) Annual Meeting in Washington, DC, U.S.

For more information about the data presented, please review the ACR/ARHP website. Also, visit Merck KGaA, Darmstadt, Germany's booth at this year's Annual Meeting to learn more about the company's commitment to advancing innovation in lupus and other immunological diseases.

**About Atacicept**
Atacicept is a potential treatment for systemic lupus erythematosus (SLE). Atacicept, a recombinant fusion protein, contains the soluble TACI receptor that binds to the cytokines BLyS and APRIL. These cytokines are members of the tumor necrosis factor family that promote B-cell survival and autoantibody production associated with certain autoimmune diseases such as SLE. Atacicept has been shown in animal models to affect several stages of B-cell development and may inhibit the survival of cells responsible for making antibodies. Merck KGaA, Darmstadt, Germany acquired exclusive worldwide development and commercialization rights for atacicept, including in North America, from Zymogenetics (acquired by Bristol-Myers Squibb) in 2008. Atacicept is currently under clinical investigation and not approved for any use in the United States, Canada and Europe.

**About Systemic Lupus Erythematosus (SLE)**
SLE (often referred to as "lupus") is a chronic autoimmune disease, where the immune system attacks the body's own tissues and organs. SLE can result in swollen, painful joints, skin rash, extreme fatigue and kidney damage. Estimates vary widely, but SLE may affect as many as 300,000 patients in the U.S. alone. Women and individuals with African American, Asian, and Hispanic heritage are affected disproportionately by SLE.



**About EMD Serono, Inc.**
EMD Serono is the biopharma business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has more than 1,100 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts.

**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.