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News Release

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ACR Abstract #
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Merck KGaA, Darmstadt, Germany Presents Late Breaking Clinical Data from Phase II Trial of Sprifermin for Osteoarthritis Disease Modification

- **Late-breaking presentation at the 2017 American College of Rheumatology/Association of Rheumatology Health Professionals Annual Meeting (ACR/ARHP) provides data on cartilage thickness in patients with knee osteoarthritis**
- **Additional data at ACR/ARHP highlights the momentum of the company's clinical programs in systemic lupus erythematosus (SLE), osteoarthritis (OA), rheumatoid arthritis (RA) and fibrotic diseases**

Darmstadt, Germany, November 4, 2017 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced results of the two-year primary analysis of FORWARD, a five-year, multicenter Phase II study of sprifermin in patients with knee OA.

"We are highly encouraged by the results of the FORWARD trial, in which sprifermin showed an increase in cartilage thickness in patients with osteoarthritis," said Luciano Rossetti, Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "We remain steadfast in our resolve to bring new therapies to areas of high unmet medical need such as this, and these phase II data are a testament to our commitment."

The study of 549 patients met its primary endpoint, demonstrating statistically-significant, dose-dependent increases in MRI total femorotibial joint cartilage thickness from baseline in the two sprifermin groups receiving the highest doses

as compared with the placebo group after the two-year treatment period (+0.03 mm with 100µg sprifermin every six months vs. -0.02 mm with placebo, $p<0.001$; +0.02 mm with 100µg sprifermin every twelve months vs. -0.02 mm with placebo, $p<0.001$). Demonstration of an increase in cartilage thickness as opposed to a delay in decreasing cartilage thickness has not been previously reported. The correlation of these changes with clinical endpoints is being evaluated.

"Osteoarthritis of the knee can make it challenging for sufferers to perform everyday activities, such as walking or climbing stairs, and there is a high unmet need for disease-modifying treatment options," said Dr. Marc C. Hochberg, primary investigator of the FORWARD study and Division Head, Rheumatology and Clinical Immunology, University of Maryland School of Medicine. "These data suggest sprifermin may not only prevent decline in cartilage thickness compared with placebo, but may also increase cartilage thickness in patients with knee osteoarthritis."

Secondary endpoints included changes in cartilage thickness as measured by MRI in the medial and lateral compartments, as well as changes in the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score over two years. Statistically significant treatment effects of increased cartilage thickness were observed in the medial and lateral femorotibial compartments, including the central medial and central lateral regions, in the highest sprifermin dose group. Total WOMAC scores decreased (indicating less symptoms) by approximately 50 percent compared to baseline in all treatment groups, including placebo.

There was no detectable systemic exposure following the intra-articular injections of sprifermin. Treatment-emergent adverse events were balanced between treatment groups, with musculoskeletal and connective tissue disorders being the most common.

The results will be presented in a late-breaking oral presentation, "Efficacy and Safety of Intra-Articular Sprifermin in Symptomatic Radiographic Knee Osteoarthritis: Results of the 2-Year Primary Analysis from a 5-Year Randomised, Placebo-Controlled, Phase II Study" at the 2017 ACR/ARHP Annual Meeting in San Diego, U.S., on Tuesday, November 7, at 4:30 p.m. PT.

The company is presenting a total of 11 abstracts at ACR/ARHP, highlighting the momentum of its various clinical programs in Immunology. Other data of note includes an oral presentation on a phase II post-hoc study analysis of atacicept for SLE patients with high disease activity. In the analysis of ADDRESS II, a 24-week, randomized, placebo-controlled Phase IIb study of 306 people, those who had high disease activity at baseline had three- to five- times the odds of attaining low disease activity at 24 weeks when treated with atacicept 150mg dose (n=51) as compared to when treated with placebo (n=52).

For more information about the data presented, please visit the ACR/ARHP website.

About Sprifermin
Sprifermin is in clinical development to investigate its potential as a treatment for osteoarthritis (OA) in the knee. It is a truncated recombinant human FGF-18 protein thought to induce chondrocyte proliferation and increased extra-cellular matrix (ECM) production, with the potential of promoting cartilage growth and repair. Sprifermin is currently in Phase II studies.

About Osteoarthritis
There are approximately 237 million people worldwide living with symptomatic and activity-limiting OA, the third most rapidly rising condition associated with disability globally. By the end stage of the disease, total knee replacement is often necessary. OA is likely to be the number one cause of total hip and knee replacement in the US. Currently there are no approved drugs for preventing or slowing disease progression.

About Atacicept
Atacicept is in clinical development to investigate its potential as a treatment for systemic lupus erythematosus (SLE). It is a recombinant fusion protein which targets the cytokines APRIL and BlyS, two members of the tumor necrosis factor family that regulates B-cell maturation, function and 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. It is currently in Phase II studies.

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 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.

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.
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