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News Release

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Merck KGaA, Darmstadt, Germany, Presents New Osteoarthritis Data at OARSI 2018 World Congress

- **Company to present 16 abstracts highlighting the momentum of its progress in osteoarthritis (OA) research and showcasing the company's leading OA pipeline**
- **Oral presentations on sprifermin offer further insights supporting its dose-response structural effect in patients with knee OA, observed in earlier studies**

Darmstadt, Germany, April 16, 2018 – 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 16 abstracts, including two oral presentations, will be presented at the Osteoarthritis Research Society International (OARSI) 2018 World Congress, held April 26-29, 2018 in Liverpool, United Kingdom. The presence of Merck KGaA, Darmstadt, Germany at OARSI reflects the company's dedication to helping optimize outcomes for patients living with chronic progressive diseases, with the goal of developing novel disease-modifying therapies for osteoarthritis (OA).

Data of note includes an oral presentation of the three-year analysis of FORWARD, a five-year, multicenter Phase II study of sprifermin in OA of the knee. Results were consistent with the two-year results, which showed a statistically significant dose-dependent increase in cartilage thickness in total, lateral and medial femorotibial compartments as compared to placebo treatment, based on quantitative magnetic resonance imaging (qMRI). At year three, which was eighteen months after the last treatment cycle, cartilage thickness declined in all treatment arms as compared to year two. However, the difference observed at year two with sprifermin at the

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highest dose and frequency versus placebo was maintained at year three. The safety profile at year three was consistent with results observed at year two, where treatment emergent adverse events were balanced between groups and musculoskeletal and connective tissue disorders the most common.

"These data suggest the structural benefit of sprifermin at the highest dose was maintained in the third year and its long-term potential as a disease-modifying treatment for osteoarthritis will continue to be explored," said Dr. Marc C. Hochberg, primary investigator of the FORWARD study and Division Head, Rheumatology and Clinical Immunology, University of Maryland School of Medicine. "Osteoarthritis impacts an estimated 10 percent of the world's population over the age of 60[1] and represents an area of high unmet need for disease-modifying treatment options."

A second oral presentation features the results of an ex vivo study that showed sprifermin induced extra-cellular matrix remodelling and cartilage regeneration. In the study, long-term treatment with sprifermin continuously increased metabolic activity and type II collagen formation in human OA articular cartilage compared with placebo.

"We are committed to helping patients with osteoarthritis by elevating our understanding of the disease and continuing to invest in highly-targeted therapies," said Luciano Rossetti, Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt Germany. "Our intent is to provide true advancement to the field of osteoarthritis by developing therapeutic options with disease-modifying potential."

Additional presentations include: pre-clinical data for M6495, an ADAMTS-5 inhibiting nanobody moving into Phase I clinical development for OA; pre-clinical data for M1673, a GDF5 mutant for the potential treatment of OA; and research related to improving measures and patient recruitment in OA studies.

Accepted abstracts at the OARSI 2018 World Congress include:

Title	Presenting Author	Abstract Number	Presentation Date/Time	Session Type/Title
Sprifermin				
Efficacy and Safety of Intra-Articular Sprifermin in	M Hochberg	32	Friday, April 27, 2:30 PM – 4:00 PM	Concurrent Session 3 –

Symptomatic Radiographic Knee Osteoarthritis: Pre-Specified Analysis of 3-Year Data From a 5-Year Randomized, Placebo-Controlled, Phase II Study with a 2 Year Treatment Phase				OA Clinical Trials and Treatment (Oral)
Articular Cartilage from OA Patients Show Extracellular Matrix Remodelling Over the Course of Treatment with Sprifermin (Recombinant Human Fibroblast Growth Factor 18)	A Bay-Jensen	65	Saturday, April 28, 10:45 AM – 12:15 PM	Plenary Session 5 – Growth Factors in OA: Opportunities for Intervention (Oral)
Intra-Articular Sprifermin Reduces Cartilage Loss in Addition to Increasing Cartilage Gain Independent of Femorotibial Location: A Post Hoc Analysis of a Randomized, Placebo-Controlled Phase II Clinical Trial	F Eckstein	551	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
M6495 (ADAMTS-5)				
In Vitro Characterization of the ADAMTS-5 Specific Nanobody M6495	D Werkmann	346	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3
Structural and Symptomatic Benefit of a Half-Live Extended Systemically Applied Anti-ADAMTS-5 Inhibitor M6495	C Brenneis	563	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Pharmacokinetic and Pharmacodynamic Modelling of the Novel Anti-ADAMTS-5 Nanobody M6495 Using the Neo-Epitope Args as a Biomarker	J Pereira	343	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
The Anti-ADAMTS-5 Nanobody, M6495, Protects Against Cartilage Breakdown in Cartilage and Synovial Joint Tissue Explant Models	A Siebuhr	363	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Study Design of a Phase I, Placebo-Controlled, First-In-Human Trial To Assess Safety and Tolerability,	A Bihlet	522	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM	Poster Sessions 1-3

Immunogenecity, and Pharmacokinetics and Pharmacodynamics of Single Ascending Doses of the Anti-ADAMTS-5 Nanobody, M6495, in Healthy Male Subjects			Saturday, April 28, 4:15 – 5:00 PM	
M1673 (GDF5 mutant)				
M1673 (GDF5 mutant) Increases Matrix Production in Primary Porcine and Human Osteoarthritic Chondrocytes	T Mang	138	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3
A GDF5 Mutant Induces Chondrogenesis in Mesenchymal Stem Cells Similarly to GDF5 Wildtype But Shows a Decreased Osteogenic Potential	T Mang	125	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Osteoarthritis Research				
C1M, C2M, C3M, PRO-C2, and CRPM in Serum Reflect Different Potential Pathogenetic Domains of Osteoarthritis, Data from Check	A Bay-Jensen	349	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Recruitment Procedure Maximising Inclusion of Progressors in OA Clinical Studies Based on Existing Cohorts: Approach-Consortium Data Analysis	P Widera	521	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Data Harmonisation for Machine Learning Model in APPROACH-consortium: Development to Predict Osteoarthritis Progression in Patients across Populations	P Widera	519	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
"APPROACH" Study: A 2-Year, European, Cohort Study to Describe, Validate and Predict Phenotypes of Knee Osteoarthritis By Use Of Clinical, Imaging and Biochemical Markers	E van Helvoort	515	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Two Year Tibiofemoral Joint Cartilage Loss is Weakly Correlated With Increased Pain Among Knees With Lower Baseline Cartilage Thickness	C Kwoh	474	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3

Pain Medication Reporting and Patient-Reported Outcomes in the Years Prior to Knee Replacement: Challenges to Assessing Symptomatic Experiences	C Kwoh	455	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3

For more information about the data to be presented, please access the OARSI app. Also, visit the Merck KGaA, Darmstadt Germany booth at this year's Congress to learn more about the company's commitment to advancing innovation in OA.

About Sprifermin
Sprifermin is in clinical development to investigate its potential as a treatment for osteoarthritis (OA) of 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 M6495
M6495 is in clinical development to investigate its potential as a treatment for osteoarthritis (OA). Administered subcutaneously, M6495 is a selective nanobody thought to inhibit a disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS-5), a metalloproteinase crucial for cartilage matrix destruction as an early and key event in developing OA, with the potential for providing structural improvement and rapid pain relief for all OA joints. M6495 is currently being evaluated in a first-in-man Phase I study in healthy subjects.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. More than 52,000 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.

[1] Arthritis Facts & Figures. Arthritis Foundation. https://www.arthritis.org/Documents/Sections/About-Arthritis/arthritis-facts-stats-figures.pdf. Accessed 12 March 2018.