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News Release

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Initiation of New Patients on Evobrutinib Paused in the U.S.; Fully Enrolled Phase III Evobrutinib Studies Continue

Darmstadt, Germany, April 12, 2023 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced the U.S. Food and Drug Administration (FDA) has placed a partial clinical hold on the initiation of new patients on evobrutinib and patients with less than 70 days exposure to study medication in the U.S. The ongoing, fully-enrolled Phase III EVOLUTION clinical trial program of evobrutinib in relapsing multiple sclerosis (RMS) will continue as planned with all participants remaining on treatment as all are beyond 70 days exposure to study medication.

The Phase III clinical trial program of evobrutinib is on schedule to read out in the fourth quarter of 2023.

The FDA action was based on their assessment of two recently reported cases of laboratory values suggestive of drug-induced liver injury that have been identified during the Phase III studies. Importantly, both patients were asymptomatic, did not require any medical intervention or hospitalization for this condition and their liver enzymes fully normalized after discontinuation of the study medication.

The Phase III EVOLUTION clinical trial program of evobrutinib has been closely monitored by an Independent Data Monitoring Committee, including hepatologists,

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since initiation. In close collaboration with external experts as well as the Independent Data Monitoring Committee for the trials, Merck KGaA, Darmstadt, Germany is assessing the potential contributory role of predisposing factors to the liver injury.

Merck KGaA, Darmstadt, Germany is working closely with the FDA to establish the best path forward for the benefit of patients in current and future trials with evobrutinib.

About Evobrutinib
Evobrutinib is an oral, CNS-penetrating, highly selective inhibitor of Bruton's tyrosine kinase (BTK) in clinical development as a potential treatment for relapsing multiple sclerosis (RMS). It is the first BTK inhibitor (BTKi) to demonstrate clinical efficacy in the largest Phase II study with follow-up beyond three years as well as demonstrate an impact on early biomarkers of ongoing central inflammation that correlate with disease progression, including slowly expanding lesions (SEL) volume and levels of blood neurofilament light chain protein (NfL). Evobrutinib is designed to modulate B cell responses such as proliferation and antibody and cytokine release, as well as modulate macrophage/microglia activation. During Phase II, the BTKi dose finding study demonstrated that BID dosing achieved maximal efficacy with >95% BTK occupancy maintained in 98% of patients before the next dose. Evobrutinib is currently under clinical investigation and is not approved for any use anywhere in the world.

Merck KGaA, Darmstadt, Germany in Neurology and Immunology
Merck KGaA, Darmstadt, Germany has a long-standing legacy in neurology and immunology, with significant R&D and commercial experience in multiple sclerosis (MS). The company's current MS portfolio includes two products for the treatment of relapsing MS – Rebif® (interferon beta-1a) and MAVENCLAD® (cladribine) tablets. Merck KGaA, Darmstadt, Germany aims to improve the lives of patients by addressing areas of unmet medical needs. In addition to Merck KGaA, Darmstadt, Germany's commitment to MS, the company also has a pipeline focusing on discovering new therapies that have potential in other neuroinflammatory and immune-mediated diseases, including systemic lupus erythematosus (SLE), generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD).

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 64,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From providing products and services that accelerate drug development and manufacturing as well as discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2022, Merck KGaA, Darmstadt, Germany, generated sales of € 22.2 billion in 66 countries.
The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.