

News Release

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Merck KGaA, Darmstadt, Germany Provides Update on Phase III Results for Evobrutinib in Relapsing Multiple Sclerosis

- **Results from the EVOLUTION clinical trials showed evobrutinib did not meet its primary endpoint of annualized relapse rate for up to 156 weeks compared to oral teriflunomide in both studies**

Darmstadt, Germany, December 5, 2023 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that its two Phase III EVOLUTION clinical trials (evolutionRMS 1 and evolutionRMS 2) investigating the efficacy and safety of evobrutinib did not meet their primary endpoints of reducing annualized relapse rates (ARR) in people with relapsing multiple sclerosis (RMS) compared to oral teriflunomide (0.15 vs. 0.14 in evolutionRMS 1 and 0.11 for evobrutinib and 0.11 for teriflunomide in evolutionRMS 2, p=NS in both trials). Of note, teriflunomide ARR values were lower than reported in other recent Phase III studies. The overall safety and tolerability profile was consistent with results from the previously reported Phase II trial. The Company will complete a full evaluation of the data from the EVOLUTION clinical trials and will work with investigators on the future presentation and publication of the results.

“With evobrutinib, our aim was to address the significant unmet need of smoldering MS in addition to strong relapse control for people living with this condition,” said



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Danny Bar-Zohar, Global Head of Research & Development and Chief Medical Officer for the Healthcare business sector of Merck KGaA, Darmstadt, Germany. "While we are very disappointed with the results, we continue to advance our strategy in healthcare with a focus on progressing our marketed portfolio and internal pipeline, complemented by external innovation, with the aim of bringing more medicines to patients, faster. I would like to sincerely thank all patients participating in the trials, their caregivers and our network of dedicated clinical investigators."

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). Evobrutinib is designed to modulate B cell responses such as proliferation and antibody and cytokine release, as well as modulate macrophage/microglia activation.

About the Phase III EVOLUTION Clinical Trial Program

The EVOLUTION clinical trial program consists of two randomized, parallel-group, double-blind, double-dummy, active-controlled Phase III studies of oral evobrutinib twice-daily versus oral teriflunomide once-daily in people with RMS to evaluate efficacy and safety ([evolutionRMS 1](#) and [evolutionRMS 2](#)). In the studies, patients with RMS (including relapsing-remitting MS or secondary progressive MS with relapses) were randomized 1:1 to receive either evobrutinib 45mg twice-daily and oral placebo once-daily or teriflunomide 14mg once-daily and oral placebo twice-daily for up to 156 weeks with a minimum treatment duration of 24 weeks.

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 2.8 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.

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).

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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

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key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.