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New Late-Breaking Data at EAN Indicate Evobrutinib is the First BTK Inhibitor to Report Efficacy and Safety in MS Over 108 Weeks

- **Investigational evobrutinib is the first and only Bruton's Tyrosine Kinase inhibitor to demonstrate high and sustained efficacy through 108 weeks in clinical studies**
- **No new safety signals identified in the 60 week open-label extension, consistent with data seen in more than 1,200 patients who have received evobrutinib to date, across MS and other conditions**
- **Late-breaking data presented as part of the European Academy of Neurology (EAN) Virtual Congress**

Darmstadt, Germany, May 23, 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced data on the long-term efficacy and safety profile of evobrutinib, an investigational, oral, highly selective Bruton's Tyrosine Kinase (BTK) inhibitor in adult patients with relapsing multiple sclerosis (RMS). The results from the Phase II open-label extension (OLE) study will be presented as a late-breaker at the European Academy of Neurology (EAN) 2020 Virtual Congress.

"These data demonstrate evobrutinib has a sustained and high impact on annualized relapse rate over 108 weeks," said Luciano Rossetti, Head of Global Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "Greatest efficacy was clearly associated with BTK occupancy, and this further validates our choice of dose for the Phase III program. We are also encouraged by

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evobrutinib's breadth of consistent safety data, including no increase of serious infections in more than 1,200 patients up to two years."

Annual relapse rate (ARR) results in the double-blind phase of the study were maintained over the open-label extension, with patients receiving evobrutinib 75mg BID (twice a day) in the double-blind phase showing an ARR of 0.11 (95% CI 0.04–0.25) at week 48, and of 0.12 (0.06–0.22) for the 108-week period.

The data from the Phase II study continues to demonstrate that BID dosing can achieve higher efficacy than QD dosing on clinical outcomes, as demonstrated by reduced ARR. Modelling data show that greater than 95% BTK occupancy at trough is necessary in nearly all patients to achieve highest efficacy and this can be best achieved with BID dosing.

Data previously published in the *New England Journal of Medicine* reported the findings of the Phase II study where at 24 weeks, evobrutinib significantly reduced the cumulative number of T1 Gd-enhancing lesions compared to placebo, meeting its primary endpoint. At week 48, all patients could enter the OLE which assessed the long-term efficacy and safety of evobrutinib.

"The 108-week efficacy and safety data for evobrutinib through the double-blind and the OLE period are very robust," noted Dr. Xavier Montalban, Chairman & Director Neurology-Neuroimmunology Department & Neurorehabilitation Unit, Multiple Sclerosis Centre of Catalonia (Cemcat), Vall d'Hebron University Hospital, Barcelona, Spain. "This, combined with the high selectivity of evobrutinib, suggests that evobrutinib may offer a promising approach to MS treatment."

Of 267 randomized patients, 213 completed 108 weeks of treatment (48 weeks in main study and 60 weeks in OLE). Evobrutinib was generally well-tolerated, with the safety profile maintained during the OLE including no increase in infections and overall no new safety signals identified. Consistent with evobrutinib's high selectivity, patients participating in the trial experienced no systemic side effects, such as gastrointestinal disturbances. In the Phase II trial, the most commonly

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observed adverse events of any grade associated with evobrutinib included nasopharyngitis and increases in levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lipase.

The transient elevated liver aminotransferases were restricted to the first 24 weeks following evobrutinib treatment initiation and were not observed in the OLE in patients continuing treatment with evobrutinib.

Evobrutinib is entering Phase III trials following the results of the Phase II clinical trial, which met its primary endpoint over 24 weeks of treatment. The two new trials, EVOLUTION RMS 1 and 2 are multi-center, randomised, parallel group, double-blind, double dummy, active-controlled studies of evobrutinib with teriflunomide, in participants with RMS. Each trial's primary endpoint is patients' ARR after 96 weeks of treatment. Secondary endpoints include the appearance of new or enlarging T2 lesions assessed by MRI scans and progressing disability as measured by the Expanded Disability Status Scale (EDSS).

About Evobrutinib
Evobrutinib (M2951) is in clinical development to investigate its potential as a treatment for multiple sclerosis (MS). It is an oral, highly selective inhibitor of Bruton's Tyrosine Kinase (BTK) which is important in the development and functioning of various immune cells including B lymphocytes and macrophages. Evobrutinib is designed to inhibit primary B cell responses such as proliferation and antibody and cytokine release, without directly affecting T cells. BTK inhibition is thought to suppress autoantibody-producing cells, which preclinical research suggests may be therapeutically useful in certain autoimmune diseases. The global Phase III clinical development programme evaluating evobrutinib in MS includes two pivotal studies, EVOLUTION RMS 1 and 2. Evobrutinib is currently under clinical investigation and not approved for any use anywhere in the world.

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 2.3 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, with a robust pipeline focusing on discovering new therapies that have the potential to modulate key pathogenic mechanisms in MS. Merck KGaA, Darmstadt, Germany, aims to improve the lives of those living with MS, by addressing areas of unmet medical needs.

The company's robust immunology pipeline focuses on discovering new therapies that have the potential to modulate key pathogenic mechanisms in chronic diseases such as MS, systemic lupus erythematosus (SLE) and forms of arthritis, including rheumatoid arthritis (RA) and osteoarthritis (OA).

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 57,000 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 advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 billion in 66 countries.

Scientific exploration and responsible entrepreneurship have been key to the company`s technological and scientific advances. This is how Merck KGaA, Darmstadt, Germany, has thrived since its founding in 1668. The founding family remains the majority owner of the publicly listed company. 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 business sectors of Merck KGaA, Darmstadt, Germany, operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials.