Merck KGaA
Darmstadt, Germany

News Release

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Merck KGaA, Darmstadt, Germany Aims to Double R&D Productivity in Oncology, Neurology and Immunology to Deliver more Medicines to Patients Faster

- **Company aims to launch one new product or indication every 1.5 years on average, bolstered by external innovation**
- **Phase III assets xevinapant and evobrutinib are expected to drive next wave of launches**
- **Focused leadership approach to pipeline enrichment builds on expertise in key biology and therapeutic areas as well as technological capabilities**

Darmstadt, Germany, November 21, 2022 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today shared updates on the company's healthcare research and development strategy, aimed at doubling R&D productivity. To achieve the goal of introducing one new product or major indication every 1.5 years on average, the company will focus its expertise and capabilities and leverage synergies within the existing pipeline to deliver transformative medicines in Oncology, Neurology and Immunology, augmented by an increased focus on external innovation. The company expects to maintain the output of its internal discovery engine, while more than 50% of future launches will result from external co-development partnerships and strategic in-licensing of assets for further in-

house development. The strategy was shared today at the company's R&D Update Call.

"We are driven by our ambition to accelerate the discovery, development and delivery of innovative medicines to patients with cancer and neuroinflammatory and immune-mediated diseases," said Danny Bar-Zohar, Global Head of Research & Development and Chief Medical Officer for the Healthcare business sector of Merck KGaA, Darmstadt, Germany. "With a mindset of design simplicity and resource discipline paired with agility of execution, we will speed the generation of high-quality data that will support our efforts to bring forth more medicines for more patients, faster."

To increase R&D productivity, the company will build on its established expertise in the underlying biology of its focused therapeutic areas of oncology, neurology and immunology and will leverage technological capabilities, particularly its industry-leading antibody-drug conjugate (ADC) technology.

Oncology: Synergistic Approaches to Striking Cancer at Its Core

The company's oncology research and development strategy centers on cancer DNA while building on existing leadership in key cancer types, including head and neck, urothelial and colorectal cancers. The oncology pipeline is focused on synergistic approaches targeting key pathways involved in cancer cell survival, deploying mechanisms to hit cancer at its core:

- Delivering tumor DNA-damaging payloads right to the cancer with cutting-edge ADC technology
- Preventing cancer cells from repairing DNA damage, through inhibition of the DNA damage response (DDR)
- Restoring sensitivity to apoptosis, the cells' natural death mechanism, which cancer can inhibit

The lead asset in the oncology pipeline is xevinapant, an investigational first-in-class potent oral small molecule IAP (Inhibitor of Apoptosis Protein) inhibitor being evaluated in the curative setting of locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)—an area that has not seen significant advances in treatment in the past 20 years. Xevinapant, which was in-licensed from Debiopharm

in March 2021, builds on the company's long heritage and extensive expertise in SCCHN. Based on the promising efficacy and safety profile seen in the Phase II trial and the urgent need for new treatments, the company is evaluating xevinapant in two ongoing randomized, double-blind, placebo-controlled Phase III clinical trials with the goal of transforming the standard of care: the TrilynX study (NCT04459715) in patients with unresected LA SCCHN, and the XRay Vision study (NCT05386550) in patients with resected LA SCCHN who are at high risk of relapse and are ineligible for cisplatin. Additional external studies and real-world evidence are expected to elucidate the potential for xevinapant across additional patient segments.

The company's broad portfolio of selective and potent DDR inhibitors includes several agents under development that directly inhibit DDR pathways required for cancer cell survival. By attacking the inherent genetic instability of cancer cells, these agents have the potential to exploit this weakness and tip the therapeutic balance in difficult-to-treat cancers. The oral ATR (ataxia telangiectasia and Rad3-related) inhibitor M1774, which has been designed as a potentially best-in-class molecule, is the leading DDR asset in the pipeline. Recently presented dose-escalation results showed that M1774 at its recommended dose expansion level showed pharmacologically robust exposure and a favorable safety profile. M1774 has broad potential in combination with other DDR inhibitors and other medicines, and as monotherapy in the right genomic context. The DDR portfolio also includes inhibitors of ATM (ataxia-telangiectasia mutated) and DNA-PK (DNA-dependent protein kinase) and has recently been complemented by a collaboration with Nerviano Medical Sciences with the option for a license agreement on the next-generation selective PARP1 (poly (ADP-ribose) polymerase) inhibitor NMS-293.

Earlier this year, M9140, the first ADC developed using the company's own technology, advanced into human trials. The ongoing Phase Ia study is assessing M9140 in patients with colorectal cancer. M9140 is an anti-CEACAM5 ADC with a topoisomerase 1 inhibitor (exatecan) payload that has been rationally designed for stability in circulation and superior cancer cell killing activity with a broad therapeutic window. M9140 has synergistic potential with DDR inhibition as well.

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Neurology and Immunology: Expansion Building on Strength in Neurology and Immune Biology

In neurology and immunology, Merck KGaA, Darmstadt, Germany, aims to expand its Multiple Sklerosis (MS) portfolio with evobrutinib, an investigational, oral, CNS-penetrating, highly selective inhibitor of Bruton's tyrosine kinase (BTK) with the potential to become a best-in-class treatment option for relapsing multiple sclerosis (RMS). In a Phase II study and follow-up, evobrutinib is the first BTK inhibitor (BTKi) to demonstrate sustained clinical efficacy for people with RMS through three and a half years and impact early biomarkers of ongoing central inflammation that correlate with disease progression, including slowly expanding lesions volume and levels of blood neurofilament light chain protein.

In pre-clinical studies, evobrutinib modulated both B cells and macrophages (in the periphery)/microglia (in the brain). This approach has the potential to positively impact both progression caused by relapses and silent progression occurring independent of relapse. 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. The Phase III readout for evobrutinib is expected in Q4 2023.

Merck KGaA, Darmstadt, Germany, also seeks to expand in neurology by evaluating the potential of oral cladribine in neurological diseases where inflammation is a primary driver, such as generalized myasthenia gravis.

The company is looking to diversify the pipeline with immunology and accelerate R&D by focusing on targets with proven biology via novel modalities. Key to these efforts is the ongoing Phase II WILLOW study of the TLR7/8 inhibitor enpatoran in cutaneous and systemic lupus erythematosus. Building on expertise in neurology, the company is initiating a proof-of-concept study in neuromuscular conditions dermatomyositis and polymyositis with enpatoran in 2023. These conditions have a high unmet medical need characterized by progressive muscle weakness and show lupus-like patterns of immune activation and TLR7/8 expression.

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"Patients rely on us. By building on our existing strengths and maximizing synergies within our in-house discovered pipeline and with external assets, we will secure sustainable R&D productivity that leads to innovative medicines for patients in need," Bar-Zohar added.

To access the presentation and a recording, please visit the company's website at https://www.emdgroup.com/en/investors/events-and-presentations.html

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 60,000 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 2021, Merck KGaA, Darmstadt, Germany, generated sales of € 19.7 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.