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Your Contact
Media Relations
noelle.piscitelli@emdserono.com
Phone: +1 (781) 427-4351

Investor Relations
investor.relations@emdgroup.com
Phone: +49 6151 72-3321

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Merck KGaA, Darmstadt, Germany's Innovative Oncology Pipeline of DNA Damage Response Inhibitors and Antibody-Drug Conjugates Poised to Advance Cancer Treatment

- **Potential best-in-class ATR inhibitor tuvusertib being explored in Phase II combination clinical studies; recently licensed PARP1 inhibitor M9466 to be evaluated in Phase Ib combination dose-finding studies**
- **Potential first-in-class anti-CEACAM5 ADC with an exatecan payload, M9140, which entered Phase Ib in colorectal cancer this year, to be explored in other CEACAM5-expressing tumors beginning in 2025**
- **First-in-class anti-GD2 ADC M3554, leveraging company's novel exatecan-based technology, set to enter first-in-human study in adults in 2024 and in pediatric patients in 2025**

Darmstadt, Germany, June 3, 2024 – Merck KGaA, Darmstadt, Germany, a leading science and technology company that operates its Healthcare business as EMD Serono in the US and Canada, today shared updates on the company's oncology pipeline and focused approach to the research and development of potential new medicines designed to improve the futures of people with cancer. This year, the company plans to open multiple new Phase Ib and II clinical studies for tuvusertib and M9466, key assets from its broad portfolio of DNA damage response (DDR) inhibitors; has advanced its lead antibody-drug conjugate (ADC), M9140, to Phase

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Ib based on positive signs of clinical benefit, and plans to expand to additional tumors; and progress M3554, its next ADC based on the company's proprietary exatecan-payload platform, into clinical development. These and other updates were shared at the company's Oncology R&D Update Call.

"The advancements in our strong early-stage clinical pipeline of ADCs created with our in-house platform and DDR inhibitors are grounded in encouraging data, particularly for M9140 and tuvusertib. The addition of M9466 to our pipeline further supports our focus on synergistic approaches in oncology, with the potential for combination with tuvusertib as well as with multiple other modalities," said Danny Bar-Zohar, Global Head of Research & Development and Chief Medical Officer for the Healthcare business sector of Merck KGaA, Darmstadt, Germany. "With our preclinical research programs in ADCs, DDR inhibitors, next-generation immuno-oncology compounds and oncogenic signaling assets, we are well-positioned to continue to fuel our clinical development efforts as we work to improve the futures of people touched by cancer."

Realizing the Full Potential of DNA Damage Response Inhibition

The company's leading pipeline of DDR inhibitors is being investigated across core hypotheses including synthetic lethality, activation of immune response, and synergy with cytotoxic drugs, to identify relevant combinations and understand which cancers are most likely to respond to different treatment regimens. Four investigational DDR inhibitor medicines in clinical trials include:

- Tuvusertib (M1774), a potentially best-in-class small-molecule oral inhibitor of the ataxia telangiectasia and Rad3-related (ATR) kinase;
- M9466, a next-generation potent and selective PARP1 (poly (ADP-ribose) polymerase 1) inhibitor, recently licensed from Jiangsu Hengrui Pharmaceuticals Co. Ltd. (Hengrui);
- Lartesertib (M4076), an ataxia telangiectasia mutated (ATM) kinase inhibitor; and
- Peposertib, a DNA-PK inhibitor.

Recently presented data lay the foundation for combination Phase II studies with tuvusertib. Data from DDRiver 301 Part B presented today at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting show the ability to combine

tuvusertib at a predicted efficacious dose with the PARP inhibitor niraparib, as well as encouraging activity in PARP-pretreated ovarian cancer. These findings complement data for the first-in-class tuvusertib and lartesertib combination first presented at the American Association for Cancer Research (AACR) Annual Meeting 2024 in April. The company is exploring tuvusertib across three Phase II studies:

- Ongoing Phase Ib/II DDRiver NSCLC 322 study (NCT05882734) in combination with cemiplimab in ICI-resistant advanced non-small cell lung cancer (NSCLC) with biomarker stratification;
- Recently opened Phase II DDRiver EOC 302 study (NCT06433219) of tuvusertib plus lartesertib or niraparib in biomarker-selected PARP-resistant ovarian cancer; and
- Recently opened Phase II JAVELIN DDRiver Bladder study (NCT06424717), in combination with BAVENCIO® (avelumab) in ICI-resistant advanced urothelial cancer.

For M9466 (also known as HRS-1167), data presented during the 2024 ASCO Annual Meeting from Hengrui's first-in-human clinical trial show a favorable safety profile and promising efficacy in PARP-naïve, PARP-sensitive tumors, supporting Merck KGaA, Darmstadt, Germany's plans to further develop this investigational medicine in various combinations. The recently opened DDRiver 501 study (NCT06421935) will evaluate M9466 in combination with tuvusertib in solid tumors with relevant mutations and/or prior PARP inhibitor exposure, with a focus on castration-resistant prostate and ovarian cancers. The clinical development program will build on the company's expertise in genitourinary and gastrointestinal cancers and aims to expand the list of indications beyond the tumors shown to be sensitive to first-generation PARP inhibitors.

Driving Innovation in Antibody-Drug Conjugates

The company has developed a proprietary technology platform for the creation of exatecan-based ADCs, with M9140 the first of these to enter clinical development. M9140 utilizes an antibody specific for CEACAM5, which is highly expressed in several tumor types, and an exatecan payload joined by a β-glucuronide linker that is specifically cleaved in tumors, releasing the cytotoxic agent into the cells. In preclinical research, M9140 has shown high bystander activity, as exatecan released in the target tumor cells can kill these cells and also permeate the cell membrane

to induce cell death in neighboring cells. First-in-human data from the PROCEADE-CRC-01 clinical trial presented at the 2024 ASCO Annual Meeting show encouraging clinical activity and a manageable and predictable safety profile for M9140 in this population. Following the completion of the ongoing dose-optimization part, the company plans to assess combinations in colorectal cancer with standard-of-care agents with alternative scheduling options. A basket trial planned to launch in early 2025 will further explore M9140 monotherapy in tumors with high CEACAM5 expression, with the potential for further exploration in various combinations.

M3554 is the next ADC based on the company's platform, linking an exatecan payload with an anti-GD2 antibody. This potentially first-in-class ADC will enter its first-in-human study later in 2024. M3554 will be evaluated in patients with solid tumors with high GD2 prevalence such as neuroblastoma, where GD2 has been validated as a target as a naked antibody, as well as soft tissue sarcoma, glioblastoma and osteosarcoma.

ADCs are one of several modalities being explored in preclinical research. By maximizing the exatecan platform, delivering next-generation cytotoxins and targeted payloads, expanding into novel antigens, and discovering immune agonist ADCs, the company anticipates expansion in the organic clinical ADC portfolio over the next several years.

Guided Approach to External Innovation

Recent agreements continue to support the company's oncology strategy, guided by focus areas across research, development and commercialization. These collaborations align with the company's goal of driving over 50% of launches in the coming years with external innovation. In addition to the agreement with Hengrui for M9466, the company has executed agreements with Caris Life Sciences to support target discovery that may accelerate discovery and development of first-in-class ADCs; with Inspirna for ompenaclid, a first-in-class compound being investigated in colorectal cancer, complementing the company's expertise in this tumor type; and with Abbisko Therapeutics Co. Ltd., for pimicotinib, for which the Phase III study in tenosynovial giant cell tumor recently completed enrollment.

Advancing the Future of Cancer Care

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At Merck KGaA, Darmstadt, Germany, we strive every day to improve the futures of people living with cancer. Our research explores the full potential of promising mechanisms in cancer research, focused on synergistic approaches designed to hit cancer at its core. We are determined to maximize the impact of our standard-of-care treatments and to continue pioneering novel medicines. Our vision is to create a world where more cancer patients will become cancer survivors. Learn more at https://www.emdseronooncology.com/home.html.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. Around 63,000 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 2023, Merck KGaA, Darmstadt, Germany, generated sales of € 21 billion in 65 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.