News Release

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Merck KGaA, Darmstadt, Germany, Expands Colorectal Cancer Portfolio Through Licensing Agreement with Inspirna

- **First-in-class ompenaclid (RGX-202) currently in Phase II development for RAS-mutated advanced or metastatic colorectal cancer**
- **Collaboration includes exclusive license outside the US with option to co-develop and co-promote ompenaclid in the US, as well as global co-development and co-commercialization rights for follow-on compounds**
- **Strategic agreement builds on the heritage of ERBITUX® (cetuximab) and complements the company's expertise and ongoing development programs in colorectal cancer**

Darmstadt, Germany, January 4, 2023 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced a licensing agreement with Inspirna, Inc. (New York, NY) for ompenaclid (RGX-202), a first-in-class oral inhibitor of the creatine transport channel SLC6A8, and SLC6A8-targeting follow-on compounds. Ompenaclid is currently being evaluated in a Phase II study for the second-line treatment of RAS-mutated (RASmut) advanced or metastatic colorectal cancer (mCRC).

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"Over the past decade, the treatment paradigm for patients with RAS-mutated CRC, accounting for approximately 45% of the second-line population, has not seen major innovation," said Victoria Zazulina, MD, Head, Development Unit, Oncology for the Healthcare business sector of Merck KGaA, Darmstadt, Germany. "With our expertise in the treatment of CRC, and based on the encouraging early data for ompenaclid, this agreement with Inspirna offers the opportunity to advance a potential new first-in-class therapy that may improve outcomes for patients."

Ompenaclid is a first-in-class oral inhibitor of the creatine transport channel SLC6A8. Data from the Phase Ib/II study of ompenaclid in combination with FOLFIRI and bevacizumab showed encouraging efficacy and safety for second-line treatment of RASmut mCRC. Results presented at the 2023 European Society for Medical Oncology (ESMO) Congress showed that, as of the September 18, 2023 data cutoff, median progression-free survival was 10.2 months and median overall survival was 19.1 months across all 41 patients with RASmut mCRC. Of the 30 patients evaluable for response, the objective response rate was 37%, with 11 partial responses. Ompenaclid was well-tolerated, with no dose-limiting toxicities observed in the dose-escalation cohort and combination safety profile comparable to FOLFIRI plus bevacizumab backbone treatment. Inspirna has initiated a Phase II double-blind randomized controlled trial in second-line RAS-mutant advanced or metastatic CRC comparing ompenaclid versus placebo plus FOLFIRI and bevacizumab.

The collaboration with Inspirna builds on Merck KGaA, Darmstadt, Germany's long-standing commitment to the colorectal cancer community. 2024 marks the 20th anniversary of the introduction of ERBITUX®, for which the company has marketing rights outside the U.S. and Canada, as a backbone treatment in mCRC; today, multiple active clinical trials continue to evaluate ERBITUX® in this disease. The company is also developing M9140, a CEACAM5-targeting antibody-drug conjugate with an exatecan payload currently being evaluated in an ongoing Phase Ia/b study in patients with mCRC.

"We are excited to partner with Merck KGaA, Darmstadt, Germany, a leader in the oncology field with global drug development and commercial expertise in colorectal cancer specifically, to help bring our novel therapies to more patients in need," said Dr. Usman "Oz" Azam, MD, Chief Executive Officer of Inspirna. "The data to date

validates our belief in ompenaclid as a potential first-in-class therapy for advanced colorectal cancer and underscores the power of our proprietary target discovery platform RNA-DRIVEr™. We look forward to working closely with Merck KGaA, Darmstadt, Germany, as we continue to evaluate ompenaclid in the ongoing Phase II randomized controlled trial."

Under the terms of the license agreement, Merck KGaA, Darmstadt, Germany will receive an exclusive license to ompenaclid outside of the United States and an option to co-develop and co-promote ompenaclid in the US. Furthermore, the parties agreed to collaborate on Inspirna's SLC6A8 follow-on compounds for which Inspirna will retain US co-development and co-commercialization rights. Inspirna will receive an upfront payment of $45 million. Upon the achievement of certain development and sales milestones for ompenaclid, Inspirna is eligible to receive milestone payments with tiered royalty rates in the low teens on net sales outside of the US. Inspirna is eligible to also receive development, regulatory and sales milestone payments for each follow-on compound targeting SLC6A8 along with up to double-digit royalties on net sales outside of the US.

About ERBITUX® (cetuximab)
ERBITUX is an IgG1 monoclonal antibody targeting the epidermal growth factor receptor (EGFR). As a monoclonal antibody, the mode of action of ERBITUX is distinct from standard non-selective chemotherapy treatments in that it specifically targets and binds to the EGFR. This binding inhibits the activation of the receptor and the subsequent signal-transduction pathway, which results in reducing both the invasion of normal tissues by tumor cells and the spread of tumors to new sites. It is also believed to inhibit the ability of tumor cells to repair the damage caused by chemotherapy and radiotherapy and to inhibit the formation of new blood vessels inside tumors, which appears to lead to an overall suppression of tumor growth. Based on in vitro evidence, ERBITUX also targets cytotoxic immune effector cells towards EGFR-expressing tumor cells (antibody-dependent cell-mediated cytotoxicity [ADCC]).
ERBITUX has already obtained market authorization in over 100 countries worldwide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck. Merck KGaA, Darmstadt, Germany licensed the right to market ERBITUX, a registered trademark of ImClone LLC, outside the U.S. and Canada from ImClone LLC, a wholly owned subsidiary of Eli Lilly and Company, in 1998.

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.

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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.