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News Release

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Merck KGaA, Darmstadt, Germany, to Collaborate with Sysmex Inostics on a Blood-Based RAS Biomarker Test

- **Development and commercialization agreement on blood-based RAS biomarker mutation status test for (metastatic) colorectal cancer (mCRC)**
- **This non-invasive, fast and easy-to-perform diagnostic test is expected to provide a real-time reflection of a patient's RAS mutation status to help guide clinical decision making in mCRC**

Darmstadt, Germany, June 1, 2014 – Merck KGaA, Darmstadt, Germany, announced today that the company has signed an agreement to collaborate with Sysmex Inostics GmbH, Hamburg, Germany, for the development and commercialization of a blood-based RAS biomarker test for patients with metastatic colorectal cancer (mCRC). This global agreement was formally signed at a ceremony coinciding with the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, U.S.

Blood-based biomarker testing is a faster and easier approach for determining the mutation status of tumors as it requires a small blood sample rather than a tissue biopsy procedure.¹ The test has the potential to provide mutation status results within days, which in turn can help guide treatment decisions.¹ In addition, it may become the method of choice where a tissue biopsy is difficult to obtain, for example in patients whose physical condition does not allow for a surgical procedure.

Merck KGaA

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News Release

“We are delighted to announce our strategic partnership with Sysmex Inostics,” said Belén Garijo, President and CEO of the company’s biopharmaceutical division. “As a company, we have embraced the principles of personalized medicine and predictive biomarkers. This collaboration reflects our commitment to leveraging our expertise in personalized medicine and predictive biomarkers in order to enhance Erbitux’s value proposition for patients, physicians and payers.”

“We are looking forward to this important collaboration with Germany’s Merck KGaA, Darmstadt, Germany, and to bringing our innovative technology to mCRC patients,” said Fernando Andreu, CEO of Sysmex Inostics. “Together, with our non-invasive, blood-based diagnostics and our new partners’ expertise in personalized medicine, we will open up new possibilities to advance biomarker testing in mCRC. This collaboration is another major step in enhancing the clinical value of Sysmex Inostics’s OncoBEAM tests and exemplifies Sysmex’s overall strategy to bring sensitive blood-based testing to the Oncology field.”

A biomarker test is a simple way of looking at the type and status of particular genes of interest in a cancer.^{2,3} Biomarkers have been found for many different types of cancer such as colorectal, breast and lung cancer, and have an increasingly important role in helping physicians to tailor care and treatment for their patients, known as ‘personalized medicine’.²⁻⁴ RAS – a predictive biomarker – is a group of genes that includes KRAS and NRAS and can be used to help select the most appropriate therapy for each individual mCRC patient.⁵⁻⁹ Currently, biomarker testing has been performed with tissue taken directly from the tumor itself, requiring an invasive biopsy, to ensure that the genes from the tumor can be isolated. However, recent technological advances embraced by Sysmex using blood samples allows very small amounts of circulating tumor DNA to be isolated and tested.

“In mCRC, RAS has been identified as a key biomarker that can help predict how well mCRC patients may respond to particular treatments, making it important to know their RAS status as early as possible,” commented Professor Sabine Tejpar, Digestive



News Release

Oncology Unit, University Hospital Gasthuisberg, Leuven, Belgium. “As this test is potentially faster and easier to perform, this could mean quicker and more timely treatment decisions – supporting the ultimate goal of improved outcomes for patients.”

Approximately half of patients with mCRC have RAS wild-type tumors and half have RAS mutant tumors.¹⁰ Results from studies assessing RAS mutation status in patients with mCRC have shown that anti-epidermal growth factor receptor (EGFR) monoclonal antibody therapies, such as Erbitux (cetuximab), can improve outcomes in patients with RAS wild-type mCRC.^{5–9}

About Colorectal Cancer

Colorectal cancer (CRC) is the second most common cancer worldwide, with an estimated incidence of more than 1.36 million new cases annually.¹¹ An estimated 694,000 deaths from CRC occur worldwide every year, accounting for 8.5% of all cancer deaths and making it the fourth most common cause of death from cancer.¹¹ Almost 55% of CRC cases are diagnosed in developed regions of the world, and incidence and mortality rates are substantially higher in men than in women.¹¹

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News Release

Notes to editors

For more information on predictive biomarkers in colorectal cancer, please visit globalcancernews.com.

About Sysmex Inostics

Sysmex Inostics, a subsidiary of Sysmex Corporation, is a molecular diagnostic company whose core competency is mutation detection utilizing highly sensitive technologies such as Plasma-Sequencing and BEAMing. With BEAMing being one of the most sensitive and quantitative technologies available today for the detection of tumor specific somatic mutations in blood samples, Sysmex Inostics' BEAMing services are readily available to support clinical trials and research in oncology. Furthermore, Sysmex Inostics companion diagnostics (CDx) team offers services for the development of non-invasive plasma DNA based IVD tests supported by a growing network of partners to cover the entire IVD development process. In addition, BEAMing tests (OncoBEAM) are available through a CLIA certified laboratory for routine clinical analysis. Sysmex Inostics' headquarters are located in Hamburg, Germany and Sysmex Inostics' Clinical Laboratory is located in Baltimore, Maryland. For more information on OncoBEAM blood testing and the BEAMing technology refer to www.sysmex-inostics.com or email info@sysmex-inostics.com.

About Erbitux

Erbitux is a first-in-class and highly active 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.

The most commonly reported side effect with Erbitux is an acne-like skin rash that seems to be correlated with a good response to therapy. In approximately 5% of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in over 90 countries for the treatment of colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck (SCCHN).

Merck KGaA, Darmstadt, Germany, licensed the right to market Erbitux outside the US and Canada from ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company, in 1998. In Japan, ImClone, Bristol-Myers Squibb Company and Merck KGaA, Darmstadt, Germany, jointly develop and commercialize Erbitux. Merck KGaA, Darmstadt, Germany, has an ongoing commitment to the advancement of oncology treatment and is currently investigating novel therapies in highly targeted areas.

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About Merck KGaA, Darmstadt, Germany

Merck KGaA of Darmstadt, Germany, is a leading company for innovative and top-quality high-tech products in the pharmaceutical and chemical sectors. Its subsidiaries in Canada and the United States operate under the umbrella brand EMD. Around 38,000 employees work in 66 countries to improve the quality of life for patients, to further the success of customers and to help meet global challenges. The company generated total revenues of € 11.1 billion in 2013 with its four divisions: Biopharmaceuticals, Consumer Health, Performance Materials and Life Science Tools. Merck KGaA of Darmstadt, Germany is the world's oldest pharmaceutical and chemical company – since 1668, the name has stood for innovation, business success and responsible



News Release

entrepreneurship. Holding an approximately 70 percent interest, the founding family remains the majority owner of the company to this day.