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Merck KGaA, Darmstadt, German, Receives FDA Fast Track Designation for Evofosfamide for Treatment of Patients Living With Advanced Pancreatic Cancer

- **Evofosfamide is an investigational compound currently in Phase III trials**
- **Advanced pancreatic cancer is second indication to receive FDA fast track designation for evofosfamide**

Darmstadt, Germany, May 12, 2015 – Merck KGaA, Darmstadt, Germany, a leading company for innovative and top-quality high-tech products in healthcare, life science and performance materials today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation for the development of evofosfamide (previously known as TH-302), administered in combination with gemcitabine, for the treatment of previously untreated patients with metastatic or locally advanced unresectable pancreatic cancer. Evofosfamide is an investigational hypoxia-activated prodrug thought to be activated under severe tumor hypoxic conditions, a feature of many solid tumors. The compound, currently in Phase III trials, is being developed in collaboration with Threshold Pharmaceuticals, Inc., South San Francisco, California, U.S.A.

Merck KGaA, Darmstadt, Germany, over the past years has bolstered its growth platforms in healthcare, life science and performance materials to provide solutions in areas with high demand for innovation. In its biopharmaceuticals business, the company has strengthened its research and development activities and is increasingly counting on partnerships to optimize relevance and efficiency.

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Merck KGaA

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“We are focused on discovering and developing innovative new therapeutic options for cancers that are particularly difficult to treat,” said Luciano Rossetti, Head of Global Research and Development of the company’s biopharmaceutical business. “Many patients with pancreatic cancer present with advanced, inoperable tumors, and there are limited treatment options currently available for them. The Fast Track designation for evofosfamide in pancreatic cancer – the second indication for this compound to receive Fast Track designation from the FDA, following the granting of the designation in soft tissue sarcoma – will help to facilitate the timely development of this high-priority program for us.”

Threshold received the first Fast Track designation for the development of evofosfamide in combination with doxorubicin for the treatment of advanced soft tissue sarcoma in November 2014.

“We are pleased that evofosfamide has been granted Fast Track status for the treatment of patients living with pancreatic cancer,” said Barry Selick, Ph.D., Chief Executive Officer of Threshold Pharmaceuticals, the co-development partner of Merck KGaA, Darmstadt, Germany. “Evofosfamide is currently being studied in patients with pancreatic cancer in the MAESTRO Phase III study, and based on current projections, we expect that the number of protocol-specified events for the trial may be reached in the second half of 2015, with the results of the primary efficacy analyses to be available shortly thereafter.”

The FDA established the Fast Track designation process to facilitate the development and expedite the review of drugs intended to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs.

Pancreatic cancer is a relatively uncommon, but lethal cancer.¹ Ranked as the 12th most common cancer worldwide, it is the 7th most common cause of cancer-related death, accounting for 4% of deaths.¹ With 93–95% of patients dying from their disease within 5 years, pancreatic cancer has a low survival rate.^{2,3} There has been little improvement seen in the survival of patients with this disease over the past 30 years⁴ and there remain



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limited treatment options for pancreatic cancer.⁵ Surgery remains the only curative approach for pancreatic cancer;⁵ however, many patients (80 - 85%) present with advanced, inoperable disease.⁶ For this large group of patients ineligible for surgery, the aim of treatment is prolongation of survival and palliation of symptoms.⁷

References

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For more information on the biopharmaceuticals business of Merck KGaA, Darmstadt, Germany, in oncology, please visit: www.globalcancernews.com.

About Evofosfamide

Evofosfamide (previously known as TH-302) is an investigational hypoxia-activated prodrug that is thought to be activated under severe tumor hypoxic conditions, a feature of many solid tumors. Areas of low oxygen levels (hypoxia) in solid tumors are due to insufficient blood vessel supply. Similarly, the bone marrow of patients with hematological malignancies has also been shown, in some cases, to be severely hypoxic.

Evofosfamide is currently under evaluation in two Phase III trials: one in combination with doxorubicin versus doxorubicin alone in patients with locally advanced unresectable or metastatic soft tissue sarcoma (the TH-CR-406 trial), and the other in combination with gemcitabine versus gemcitabine and placebo in patients with locally advanced unresectable or metastatic pancreatic cancer (the MAESTRO trial). Both Phase III trials are being conducted under Special Protocol Assessment (SPA) agreements with the FDA. The FDA and the European Commission have granted evofosfamide Orphan Drug designation for the treatment of STS and pancreatic cancer. The FDA has also granted Fast Track designation for evofosfamide for both STS and pancreatic cancer. Evofosfamide is also being investigated in a Phase II trial for the treatment of non-squamous non-small cell lung cancer, and in earlier-stage clinical trials of other solid tumors and hematological malignancies.

Merck KGaA, Darmstadt, Germany, signed a global license and co-development agreement for evofosfamide with Threshold Pharmaceuticals, Inc. in February 2012, with an option for Threshold to co-commercialize in the U.S.

Evofosfamide is currently under clinical investigation and has not been approved for use in the U.S., Europe, Canada, or elsewhere. Evofosfamide has not yet been proven to be either safe or effective and any claims of safety and effectiveness can be made only after regulatory review of the data and approval of the labeled claims.



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Merck KGaA of Darmstadt, Germany, is a leading company for innovative and top-quality high-tech products in healthcare, life science and performance materials. The company has six businesses – Biopharmaceuticals, Consumer Health, Allergopharma, Biosimilars, Life Science and Performance Materials – and generated sales of € 11.3 billion in 2014. Around 39,000 employees work in 66 countries to improve the quality of life for patients, to foster the success of customers and to help meet global challenges. Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company – since 1668, the company has stood for innovation, business success and responsible entrepreneurship. Holding an approximately 70% interest, the founding family remains the majority owner of the company to this day. Merck KGaA, Darmstadt, Germany holds the global rights to the Merck name and brand. The only exceptions are Canada and the United States, where the company operates as EMD Serono, EMD Millipore and EMD Performance Materials.