ONO PHARMACEUTICAL CO.,LTD.

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Detailed Results of Phase III Trial of L-BLP25 in Patients with Non-Small Cell Lung Cancer (START) to be Presented at ASCO

Merck Serono, a division of Merck, Darmstadt, Germany, today announced detailed results from the randomized Phase III START trial of its investigational MUC1 antigen-specific cancer immunotherapy L-BLP25 (formerly referred to as Stimuvax) in patients with unresectable, locally advanced Stage III non-small cell lung cancer, which will be presented at the American Society of Clinical Oncology (ASCO) 2013 Annual Meeting in Chicago.

Attached is the press release made by Merck Serono for your information.

In Japan, a Phase II study of L-BLP25 for the treatment of non-small cell lung cancer (EMR63325-009) is being conducted by Merck Serono Co., Ltd., a Japanese subsidiary of Merck Serono, and Ono in accordance with the license agreement* signed in October 2011.

* Ono entered into a license agreement with Merck KGaA. Ono obtained rights to co-develop and co-market L-BLP25 in Japan together with Merck Serono Co., Ltd.

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ASCO Abstract Number: 7500

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Merck Serono: Detailed Results of Phase III Trial of L-BLP25 in Patients With Non-Small Cell Lung Cancer (START) to be Presented at ASCO

- **Confirmed: Primary endpoint of significantly improving overall survival not met**
- **Predefined subgroup of patients receiving initial concurrent chemoradiotherapy: median overall survival of 30.8 months observed in patients treated with L-BLP25 compared to 20.6 months in patients receiving placebo (HR 0.78, p=0.016) in post hoc analysis**
- **Detailed results to be presented on Tuesday, June 4**

Darmstadt, Germany, May 16, 2013 – Merck Serono, a division of Merck, Darmstadt, Germany, today announced detailed results from the randomized Phase III START* trial of its investigational MUC1 antigen-specific cancer immunotherapy L-BLP25 (formerly referred to as Stimuvax) in patients with unresectable, locally advanced Stage III non-small cell lung cancer (NSCLC). These results will be presented at the American Society of Clinical Oncology (ASCO) 2013 Annual Meeting in Chicago. The primary endpoint of improving overall survival (OS) was not met. In a predefined subgroup of patients receiving initial concurrent chemoradiotherapy (CRT), a combination of chemotherapy and radiotherapy given at the same time, a median overall survival of 30.8 months versus 20.6 months was observed based on a post hoc analysis in patients treated with L-BLP25 versus placebo respectively (HR 0.78, 95% CI 0.64–0.95, p=0.016, n=806). The results of the START trial will be presented during the Oral Abstract Session “Lung Cancer – Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers” from 09.45 am to 12.45 pm on Tuesday, June 4.

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The START trial is assessing the safety, efficacy and tolerability of L-BLP25 in patients with unresectable, locally advanced Stage III NSCLC who have not progressed after initial CRT, which is the current standard of care. Before receiving treatment with either L-BLP25 or placebo in the START trial, two-thirds of patients had received concurrent CRT and one-third had received sequential CRT (radiotherapy started after completion of chemotherapy). The trial did not meet its primary objective of demonstrating a significantly improved OS with L-BLP25 compared to placebo in the primary analysis study population (n=1,239). Median OS was 25.6 months for patients in the L-BLP25 group compared with 22.3 months for those in the placebo group (adjusted HR 0.88, 95% CI 0.75–1.03, p=0.123). Injection site reactions, a pre-defined group of adverse events, occurred in 17.3% of patients in the L-BLP25 group and in 11.9% of patients in the placebo group. Flu-like symptoms, another pre-defined group of adverse events, observed within 2 days after subcutaneous injection of study medication occurred in 10.9% of patients in the L-BLP25 group and in 9.9% of patients in the placebo group. Potentially immune-related diseases or events occurred at similar frequencies in both treatment groups. The most common adverse events (>10%) in subjects allocated to L-BLP25 were cough, dyspnea, fatigue, back pain, nausea, chest pain, nasopharyngitis, headache, decreased appetite and arthralgia, and in those allocated to placebo were cough, dyspnea, fatigue, back pain and headache. The most common grade 3 or 4 adverse event in both treatment groups was dyspnea (L-BLP25 group 4.8%, placebo group 4.4%).

In a post hoc analysis of the predefined subgroup of patients receiving initial concurrent CRT (n=806), patients receiving L-BLP25 had a median OS of 30.8 months compared to patients receiving placebo, who had a median OS of 20.6 months [HR 0.78; 95% CI 0.64–0.95; p=0.016]). In patients receiving sequential CRT followed by L-BLP25 or placebo a median OS of 19.4 months was observed for the L-BLP25 group compared with 24.6 months for the placebo group (n=433; HR 1.12; 95% CI 0.87–1.44; p=0.38). Predefined subgroup analyses included, among others, disease stage (IIIA or IIIB), response to initial CRT (stable disease versus objective response), type of initial CRT (concurrent versus sequential) and geographic region.

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"While the results from the primary analysis population were certainly not what we hoped for, I am encouraged by the results seen in the subgroup of patients receiving concurrent CRT followed by L-BLP25, particularly as concurrent CRT is the standard of care recommended for patients with unresectable Stage III NSCLC in both the NCCN[†] and ESMO[‡] guidelines," said Dr. Charles Butts, Cross Cancer Institute, University of Alberta, Edmonton, Canada, clinical investigator and member of the START trial's steering committee. "This is the first time that an antigen-specific cancer immunotherapy has shown this effect in a substantial subgroup of NSCLC patients who are usually only observed following chemoradiotherapy."

Dr. Annalisa Jenkins, Head of Global Drug Development and Medical for Merck Serono, said: "We believe the results from the START trial offer scientific insights to the medical community on the potential clinical utility of immunotherapy approaches in oncology. As we better understand the biology behind immune responses in patients living with cancer, our learnings can be applied to advance progress in this field."

L-BLP25 is an investigational MUC1 antigen-specific cancer immunotherapy designed to stimulate the body's immune system to identify and target cancer cells expressing the cell-surface glycoprotein MUC1.[1,2] MUC1 is expressed in many cancers, such as NSCLC, and has multiple roles in tumor growth and survival.[1,3]

Globally, lung cancer is the most common cause of cancer-related deaths in men and the second most common in women, responsible for almost twice as many deaths as both breast and prostate cancer combined.[4] NSCLC is the most common type of lung cancer, accounting for 80–85% of all lung cancers, and locally advanced or Stage III disease accounts for approximately 30% of patients with NSCLC.[5,6] Unfortunately, at diagnosis, most patients have advanced or metastatic disease with a very poor prognosis.[7] There is an especially urgent and ongoing need for new approaches for patients with advanced, unresectable NSCLC.

*START: **S**timulating **T**argeted **A**ntigenic **R**esponses **T**o NSCLC

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†NCCN guidelines: National Compendium Cancer Network Guidelines Version 2.2013 Non-Small Cell Lung Cancer

‡ESMO guidelines: Early stage and locally advanced (non-metastatic) non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

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About L-BLP25

L-BLP25 is an investigational MUC1 antigen-specific cancer immunotherapy that is designed to stimulate the body's immune system to identify and target cells expressing the cell-surface glycoprotein MUC1. MUC1 is expressed in many cancers, such as non-small cell lung cancer (NSCLC), and has multiple roles in tumor growth and survival. L-BLP25 is currently being investigated in the Phase III START and INSPIRE trials for the treatment of unresectable, locally advanced Stage III NSCLC.

Merck obtained the exclusive worldwide rights for development and commercialization of L-BLP25 from Oncothyreon Inc., Seattle, Washington, U.S., in 2007, in an agreement replacing prior collaboration and supply agreements originally entered in 2001. In Japan, Merck entered into a co-development and co-marketing agreement for L-BLP25 with Ono Pharmaceutical Co., Ltd., Osaka, Japan.

START is a Phase III, multicenter, randomized, double-blind, placebo-controlled clinical trial designed to assess the efficacy, safety and tolerability of L-BLP25 in patients suffering from unresectable, locally advanced (Stage IIIA or IIIB) NSCLC who have had a response or stable disease after at least two cycles of platinum-based chemoradiotherapy (concurrent or sequential). The trial involves 1,239 patients in 33 countries. The primary endpoint of START is overall survival.

INSPIRE (BLP25 liposome vaccine trial **I**n Asian **NS**CLC **P**atients: Stimulating **I**mmune **RE**sponse) is a Phase III, multicenter, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the efficacy, safety and tolerability of L-BLP25 in patients suffering from unresectable, locally advanced Stage IIIA or IIIB NSCLC who have had a response or stable disease after at least two cycles of platinum-based chemoradiotherapy. The design of INSPIRE is almost identical to the START trial. INSPIRE is enrolling approximately 420 unresectable, locally advanced Stage III NSCLC patients across China, Hong Kong, Korea, Singapore and Taiwan.

L-BLP25 is currently under clinical investigation and has not been approved for use in the U.S., Europe, Canada, or elsewhere. L-BLP25 has not 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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About Merck Serono

Merck Serono is the biopharmaceutical division of Merck. With headquarters in Darmstadt, Germany, Merck Serono offers leading brands in 150 countries to help patients with cancer, multiple sclerosis, infertility, endocrine and metabolic disorders as well as cardiovascular diseases. In the United States and Canada, EMD Serono operates as a separately incorporated subsidiary of Merck Serono.

Merck Serono discovers, develops, manufactures and markets prescription medicines of both chemical and biological origin in specialist indications. We have an enduring commitment to deliver novel therapies in our core focus areas of neurology, oncology, immuno-oncology and immunology.

About Merck

Merck is a leading pharmaceutical, chemical and life science company with total revenues of € 11.2 billion in 2012, a history that began in 1668, and a future shaped by approx. 39,000 employees in 66 countries. Its success is characterized by innovations from entrepreneurial employees. Merck's operating activities come under the umbrella of Merck KGaA, in which the Merck family holds an approximately 70% interest and free shareholders own the remaining approximately 30%. In 1917 the U.S. subsidiary Merck & Co. was expropriated and has been an independent company ever since.

For more information, please visit www.merckserono.com or www.merckgroup.com