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Decision to Continue the Development of Tecemotide (L-BLP25) in Non-Small Cell Lung Cancer to be Announced

Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced the decision to continue clinical development of its investigational MUC1 antigen-specific cancer immunotherapy tecemotide (L-BLP25) under a new Phase III trial (START2) for patients with unresectable, locally advanced Stage III non-small cell lung cancer (NSCLC) on September 25, 2013.

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

In Japan, a Phase II study of Tecemotide 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 Tecemotide in Japan together with Merck Serono Co., Ltd.

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News Release

September 25, 2013

Merck Serono Announces Decision to Continue the Development of Tecemotide in Stage III Non-Small Cell Lung Cancer

- **The program will build upon the data from START* trial and explore potential in patients with Stage III NSCLC who have demonstrated stable disease or objective response after concurrent chemoradiotherapy**
- **The Phase III START2 study will be conducted under a Special Protocol Assessment (SPA) with FDA**

Darmstadt, Germany, September 25, 2013 – Merck Serono, the biopharmaceutical division of Merck, today announced the decision to continue clinical development of its investigational MUC1 antigen-specific cancer immunotherapy tecemotide (also known as L-BLP25) under a new Phase III trial called START2 for patients with unresectable, locally advanced Stage III non-small cell lung cancer (NSCLC). This announcement is based on the outcome of the START trial. The START trial did not meet the primary endpoint of improving overall survival (OS) in the overall patient population. Data from an exploratory analysis of a predefined subgroup of patients in the START trial, who received tecemotide after concurrent chemoradiotherapy (CRT), showed that these patients achieved a median OS of 30.8 months versus 20.6 months in patients treated with placebo (n=806; HR: 0.78; 95% CI 0.64–0.95; p=0.016). Concurrent CRT is a combination of chemotherapy and radiotherapy given at the same time.

The START2 trial is a Phase III, multicenter, randomized, double-blind, placebo-controlled clinical trial designed to assess the efficacy, safety and tolerability of tecemotide in patients suffering from unresectable, locally advanced (Stage IIIA or IIIB)

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NSCLC who have had a response or stable disease after at least two cycles of platinum-based concurrent CRT. Concurrent CRT is the current standard of care for these patients. The trial's primary endpoint is OS. The company also announced that it has received Scientific Advice from the European Medicines Agency (EMA) on the program, and has reached an agreement with the U.S. Food and Drug Administration (FDA) on a Special Protocol Assessment (SPA) for the Phase III international randomized trial.

"The results from the START trial provided insights into the potential clinical utility of tecemotide and raised a lot of interest in the scientific community. We haven't seen this type of clinically meaningful survival benefit with any other investigational therapies in unresectable Stage III NSCLC. Further investigation might help to better understand the potential role that tecemotide could play in successfully treating these patients," said Dr. Charles Butts, Cross Cancer Institute, University of Alberta, Edmonton, Canada, clinical investigator of the START trial and member of the corresponding steering committee.

Dr. Annalisa Jenkins, Head of Global Drug Development and Medical for Merck Serono, said: "The START data delivered important insights that we believe justify further investigation in a new Phase III program. NSCLC is a devastating disease, and we are pleased to be able to continue supporting innovation in this important emerging field of immuno-oncology."

Tecemotide 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, including 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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About tecemotide

Tecemotide 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. Tecemotide 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 tecemotide 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 tecemotide with Ono Pharmaceutical Co., Ltd., Osaka, Japan.

The START2 trial is a Phase III, multicenter, randomized, double-blind, placebo-controlled clinical trial designed to assess the efficacy, safety and tolerability of tecemotide 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 concurrent chemoradiotherapy (CRT). The primary endpoint of START2 trial is overall survival.

The initial Phase III trial START is a multicenter, randomized, double-blind, placebo-controlled clinical trial designed to assess the efficacy, safety and tolerability of tecemotide 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 overall survival was not met in the START trial.

INSPIRE (tecemotide 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 tecemotide 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 concurrent 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.

Tecemotide is currently under clinical investigation and has not been approved for use in the U.S., Europe, Canada, or elsewhere. Tecemotide 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.

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

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. 38,000 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.