



## Current Agreements

### Dealdoc

#### Co-development and co-marketing agreement for Stimuvax

Merck KGaA

Ono Pharmaceutical

Oct 04 2011

## Co-development and co-marketing agreement for Stimuvax

<b>Companies:</b>	<a href="#">Merck KGaA</a> <a href="#">Ono Pharmaceutical</a>
<b>Announcement date:</b>	Oct 04 2011
<b>Deal value, US\$m:</b>	6.65 : sum of upfront payment

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### Details

<b>Announcement date:</b>	Oct 04 2011
<b>Industry sectors:</b>	Bigpharma Pharmaceutical
<b>Therapy areas:</b>	Oncology » Lung cancer
<b>Technology types:</b>	Biological compounds Vaccines Co-development
<b>Deal components:</b>	Co-market Licensing
<b>Stages of development:</b>	Phase II
<b>Geographic focus:</b>	Asia » Japan

### Financials

<b>Deal value, US\$m:</b>	6.65 : sum of upfront payment
<b>Upfront, US\$m:</b>	6.65 : upfront payment

### Termsheet

Ono will receive a co-development and co-marketing license for Stimuvax in Japan and Merck Serono will receive an upfront payment of € 5 million.

No further financial terms are disclosed.

A Phase II study for Stimuvax (EMR63325-009) is being conducted by Merck Serono Co., Ltd., a Japanese subsidiary of Merck, for the treatment of non-small cell lung cancer in Japan; Phase III studies are in progress outside Japan.

### Press Release

4 October 2011

Merck and Ono Pharmaceutical Form Collaborations to Develop Oral Multiple Sclerosis Drug and Cancer Immunotherapy

- Merck Serono to collaborate with Ono for the development and commercialization of ONO-4641, an oral investigational sphingosine-1-phosphate (S1P) receptor modulator, in Phase II in multiple sclerosis
- The companies will also collaborate in Japan on the development and marketing of Stimuvax, Merck's investigational cancer immunotherapy currently in Phase III clinical development

Darmstadt, Germany, October 4, 2011 – Merck KGaA announced today that it signed two agreements for collaboration of its Merck Serono division with Ono Pharmaceutical Co., Ltd., Osaka, Japan to strengthen its multiple sclerosis and cancer franchises.

The first agreement grants Merck worldwide exclusive license rights for the development and commercialization of ONO-4641 outside of Japan, Korea and Taiwan. ONO-4641 is a novel oral compound currently in Phase II of development that was originally discovered and developed by Ono for the potential treatment of multiple sclerosis. The second license agreement provides Ono with co-development and co-marketing rights of Stimuvax® in Japan. Stimuvax is an investigational therapeutic cancer immunotherapy designed to stimulate the body's immune system to target cancer cells that express the tumor antigen MUC-1 that is in development in Phase III for patients suffering from non-small cell lung cancer. "Merck Serono is committed to building on our leadership franchise in multiple sclerosis and we are excited about adding a potential oral treatment, ONO-4641, to our pipeline," said Stefan Oschmann, Executive Board Member of Merck and responsible for the Merck Serono division. "We also believe that Ono will bring a wealth of experience in developing innovative therapies and understanding regulatory requirements in Japan."

"We are very glad to partner with Merck Serono for the development and marketing of ONO-4641, given Merck Serono's commitment to developing treatments for people living with multiple sclerosis," said Gyo Sagara, Ono's President and Representative Director. "Moreover, we are delighted to collaborate in Japan on Stimuvax and together with Merck Serono to offer a potential future medicine for people suffering from non-small cell lung cancer."

Under the terms of the agreement for ONO-4641, Merck Serono will acquire worldwide exclusive rights, excluding Japan, Korea and Taiwan, to develop and commercialize ONO-4641. Ono will receive 1.5 billion Japanese Yen (about € 14 million) as an upfront payment and could receive additional payments based on the achievement of certain development, regulatory and commercial milestones for ONO-4641. No further financial terms are disclosed. ONO-4641 is a sphingosine-1-phosphate (S1P) receptor agonist, and the multi-national Phase II study DreaMS (Drug Research Evaluation for Multiple Sclerosis) is on-going in patients with relapsing-remitting multiple sclerosis.

Under the terms of the separate agreement for Stimuvax, Ono will receive a co-development and co-marketing license for Stimuvax in Japan and Merck Serono will receive an upfront payment of € 5 million. No further financial terms are disclosed. A Phase II study for Stimuvax (EMR63325-009) is being conducted by Merck Serono Co., Ltd., a Japanese subsidiary of Merck, for the treatment of non-small cell lung cancer in Japan; Phase III studies are in progress outside Japan. Merck obtained the exclusive worldwide licensing rights from Oncothyreon Inc., Seattle, Washington, USA.

Multiple sclerosis Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that approximately two million people have MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

Stimuvax Merck Serono is investigating the use of Stimuvax (BLP25 liposome vaccine) in the treatment of NSCLC. Merck obtained the exclusive worldwide licensing rights from Oncothyreon Inc., Seattle, Washington, USA. Stimuvax is being developed in Europe by Merck Serono. In the United States and Canada, Stimuvax is being developed by EMD Serono, an affiliate of Merck.

The START study is a Phase III, multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the efficacy, safety and tolerability of Stimuvax in subjects suffering from unresectable, stage IIIA or IIIB non-small cell lung cancer (NSCLC) who have had a response or stable disease after at least two cycles of platinum-based chemo-radiotherapy. The study will involve more than 1,500 patients in approximately 30 countries. The primary endpoint of the START study is overall survival (OS).

The INSPIRE study is a Phase III, multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the efficacy, safety and tolerability of Stimuvax in subjects suffering from unresectable, stage IIIA or IIIB non-small cell lung cancer (NSCLC) who have had a response or stable disease after at least two cycles of platinum-based chemo-radiotherapy. The design of the INSPIRE study is almost identical to the START study. INSPIRE will enrol approximately 420 unresectable, stage III NSCLC patients across China, Hong Kong, Korea, Singapore and Taiwan.

Ono Pharmaceutical Ono Pharmaceutical Co., Ltd. is a R&D-oriented pharmaceutical company specializing in creating innovative medicines in specific areas and is headquartered in Osaka, Japan. For more information about Ono, visit the company's website at [www.ono.co.jp](http://www.ono.co.jp).

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3 October 2011

Ono to Enter into License Agreements with Merck KGaA

Development and commercialization by Merck of ONO-4641 for the treatment of multiple sclerosis, worldwide except Japan, Korea and Taiwan

Co-development and co-marketing of Stimuvax®, a cancer immunotherapy, in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan, President and Representative Director: Gyo Sagara) announced today that the company signed two separate agreements with Merck KGaA (Darmstadt, Germany) on October 3, 2011 to out-license ONO-4641, a novel compound originally discovered and developed by Ono for the treatment of multiple sclerosis and to license for co-development and co-marketing Stimuvax®

(candidate for product name) in Japan, a novel cancer immunotherapy, globally developed by Merck Serono, the biopharmaceutical division of Merck KGaA. Please refer to the following explanations about details of the agreements.

#### About out-licensing agreement on ONO-4641

Ono granted Merck an exclusive license for development and commercialization of ONO-4641 in countries around the world except Japan, Korea and Taiwan. Under the terms of the agreement, Ono will receive 1.5 billion yen as an upfront payment. In addition, Ono will also receive milestone payments based on development stage as well as sales-based ones upon achievement of projected sales of ONO-4641.

ONO-4641 is a sphingosine-1-phosphate (S1P) receptor agonist, and the multi-national phase II study, DreaMS \* is on-going for the treatment of multiple sclerosis. The drug keeps lymphocytes in lymph nodes and thereby inhibits the infiltration of lymphocytes into lesions. The compound is therefore expected to be a drug for the treatment of auto-immune diseases such as multiple sclerosis, which is regarded as an intractable disease.

#### About license, co-development and co-marketing agreement on Stimuvax® in Japan

Ono obtained rights to co-develop and co-market Stimuvax® (BLP25 liposome vaccine) in Japan together with Merck. Under the terms of the agreement, Ono will pay to Merck 5 million euros as an upfront payment.

A Phase II study for Stimuvax® (EMR63325-009) is being conducted by Merck Serono Co., Ltd., a Japanese subsidiary of Merck KGaA, for the treatment of non-small cell lung cancer in Japan (Phase III studies are in progress outside Japan). Merck KGaA obtained the exclusive worldwide licensing rights from Oncocyte Inc., Seattle, Washington, USA. Stimuvax® is a cancer immunotherapy targeting the tumor antigen, MUC-1.

"We are very glad to partner with Merck Serono for the development and marketing of ONO-4641, given Merck Serono's commitment to developing treatments for people living with multiple sclerosis," said Gyo Sagara, Ono's President and Representative Director. "Moreover, we are delighted to collaborate in Japan on Stimuvax and together with Merck Serono to offer a potential future medicine for people suffering from non-small cell lung cancer."

"Merck Serono is committed to building on our leadership franchise in multiple sclerosis and we are excited about adding a potential oral treatment, ONO-4641, to our pipeline," said Dr. Stefan Oschmann, President of Merck Serono. "We also believe that Ono will bring a wealth of experience in developing innovative therapies and understanding regulatory requirements in Japan."

The impact from these license agreements on the projected business performance of this fiscal year (ending March 2012) will be immaterial.

#### About Merck Serono

Merck Serono is the biopharmaceutical division of Merck KGaA, Darmstadt, Germany, a global pharmaceutical and chemical company. Headquartered in Geneva, Switzerland, Merck Serono discovers, develops, manufactures and markets prescription medicines of both chemical and biological origin in specialist indications. In the United States and Canada, EMD Serono operates as a separately incorporated affiliate of Merck Serono.

Merck Serono has leading brands serving patients with cancer (Erbix®, cetuximab), multiple sclerosis (Rebif®, interferon beta-1a), infertility (Gonal-f®, follitropin alfa), endocrine and metabolic disorders (Saizen® and Serostim®, somatropin), (Kuvan®, sapropterin dihydrochloride), (Egrifta®, tesamorelin), as well as cardiometabolic diseases (Glucophage®, metformin), (Concor®, bisoprolol), (Euthyrox®, levothyroxine). Not all products are available in all markets.

With an annual R&D expenditure of over € 1 bn, Merck Serono is committed to growing its business in specialist-focused therapeutic areas including neurodegenerative diseases, oncology, fertility and endocrinology, as well as new areas potentially arising out of research and development in rheumatology.

#### About Merck

Merck is a global pharmaceutical and chemical company with total revenues of € 9.3 billion in 2010, a history that began in 1668, and a future shaped by more than 40,000 employees in 67 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 shareholders own the remaining approximately 30%. In 1917 the U.S. subsidiary Merck & Co. was expropriated and has been an independent company ever since.

#### About tumor antigen

It is known that an immune cell recognizes a certain type of protein or peptide expressed on the surface of cancer cells as an antigen, and then attacks cancer cells expressing the antigen. The protein or peptide which is recognized as an antigen is called "tumor antigen".

#### About multiple sclerosis

Multiple sclerosis is chronic neurological disorder accompanying diversified and severe neurological symptoms such as paralysis and numbness of limbs, gait disorder, visual disorder, dysuria. Although there are no specific factors that are known to be responsible for onset and relapse of the disease, it is thought to be one of autoimmune diseases that, because of some triggers, own body improperly recognized as foreign, is attacked by lymphocytes, which has an essential role in immune system for protection from foreign substances such as virus and bacteria. Most patients are diagnosed between the ages of 20 and 40, and women tend to suffer disproportionately from this disease compared to men. Patient number in Japan is around 12,000, but it's said that there are at least 350,000 patients in US and about 2.5 million ones all over the world.

About non-small cell lung cancer

Lung cancer is classified into two types, non-small-cell lung cancer and small-cell lung cancer. Non-small-cell lung cancer constitutes 80% of total lung cancer. In Japan, the number of deaths due to lung cancer accounts for 19.6% of total cancer death. Lung cancer is the highest frequency of cancer death in men, and is the second behind colorectal cancer in women. **Smoking is the strongest risk factor for lung cancer, and it's reported that risk of lung cancer for smokers is 4.4 times as much as that of non-smokers in men, and 2.8 times in women\*.**

\*\* "Demographics survey" (demographics statistics in 2009) by Health, Labour and Welfare Ministry

\*\*\* Homepage of "Center for Cancer Control and Information Services" by NATIONAL CANCER CENTER (incorporated administrative agency)

## Filing Data

*Not available.*

## Contract

*Not available.*