

October 30, 2007

## **Initiation of Development of “ONO-4538/MDX-1106”, Fully Human Anti-PD-1 Antibody for Hepatitis C in US**

### **– Allowance of Investigational New Drug (IND) for Addition of Hepatitis C Treatment to Ongoing Oncology Program for ONO-4538/MDX-1106 –**

October 30, 2007 – Ono Pharmaceutical Co., Ltd. (Head Office: Osaka, President: Toshiharu Korekane) and Medarex, Inc. (Head Office: New Jersey, President and CEO: Howard Pien) announced today the initiation of development of “ONO-4538/MDX-1106”, a fully human anti-PD-1 antibody under investigation for treatment of hepatitis C in the US. ONO-4538/MDX-1106 was developed under the May 2005 collaborative research agreement between Ono and Medarex, and currently is in a separate ongoing Phase I clinical study being conducted in patients with recurrent or treatment-refractory cancer in the US.

The investigational new drug application (IND) filed with the U.S. Food & Drug Administration (FDA) by Medarex for a Phase I study in patients with hepatitis C with ONO-4538/MDX-1106 was recently accepted. The Phase I single-dose, dose-escalation trial with ONO-4538/MDX-1106 is expected to enroll up to 34 patients with active hepatitis C genotype 1 infection. The study is intended to evaluate the safety, pharmacokinetics, and preliminary efficacy of single doses of ONO-4538/MDX-1106.

The two companies plan to share the development costs up to the completion of a Phase II clinical study. After the establishment of POC (Proof of Concept: proof of efficacy in human), each company will be responsible for any continued development in its exclusive territory; Medarex's exclusive territory is North America, and Ono's exclusive territory is all countries outside of North America.

“Recently, involvement of PD-1 in hepatitis C has been reported in the scientific literature. ONO-4538/MDX-1106 aims to improve the immune capacity of the body and treat hepatitis C by inhibiting involvement of PD-1, which is a novel mechanism of action. We are seeking to develop ONO-4538/MDX-1106 to be a new treatment for hepatitis C,” said Shozo Matsuoka, Ph.D., Senior Managing Director of Ono Pharmaceutical, Co., Ltd.

“We value our partnership with Ono and are pleased with the progress to study the potential of ONO-4538/MDX-1106 in both oncology and infectious diseases,” said Howard Pien, President and CEO of Medarex. “We believe that our ongoing program in patients with cancer is currently progressing well and that this exploratory Phase I study in HCV may be a step toward potentially adding new infectious disease indications for therapeutic blockade of this important T cell regulatory molecule.”

Ono and Medarex plan to continue to investigate the potential of ONO-4538/MDX-1106 collaboratively for cancer in a separate ongoing Phase I clinical trial and for hepatitis C.

#### About ONO-4538/MDX-1106

PD-1 (programmed cell death 1) is one of the receptors expressed on the surface of activated lymphocytes (T-cells) and is involved in the system of negative regulation for the suppression of activated lymphocytes. An increasing number of studies have reported that tumor cells and certain chronic viruses, including HCV and HIV, may use the PD-1 pathway to evade host adaptive immune responses (which protect the host from both harmful pathogens and tumors), suggesting that blockade of the negative regulatory signal mediated by PD-1 is expected to promote the host immune response to recognize tumor cells and viral pathogens as foreign and eliminate them. Preclinical studies suggest that blockade of the PD-1 signaling pathway by ONO-4538/MDX-1106, a fully human anti-PD-1 antibody, activates T-cell responses and promotes an immune response to fight tumors and infectious diseases.

#### Collaborative Research Agreement with Medarex

In May 2005, Ono entered into a collaboration agreement with Medarex to research and develop a fully human anti-PD-1 antibody for the treatment of cancer. Under this agreement, Ono's intellectual property regarding PD-1 (gene) and Medarex's "UltiMAb®", a technology to develop human antibody, are combined for commercialization of an anti-PD-1 antibody. The two companies plan to share the development costs up to the completion of a Phase II clinical study. After the establishment of POC (Proof of Concept: proof of efficacy in human), each company will be responsible for any continued development in its exclusive territory; Medarex's exclusive territory is North America, and Ono's exclusive territory is all countries outside of North America.

A Phase I clinical study in patients with recurrent or treatment-refractory cancer with "ONO-4538/MDX-1106", a fully human anti-PD-1 antibody developed under a collaborative research agreement between Ono and Medarex, is conducted in the US by Medarex.

#### About Medarex

Medarex is a biopharmaceutical company focused on the discovery, development and potential commercialization of fully human antibody-based therapeutics to treat life-threatening and debilitating diseases, including cancer, inflammation, autoimmune disorders and infectious diseases. More than 30 of these therapeutic product candidates derived from Medarex technology are in human clinical testing or have had INDs submitted for such trials, with seven of the most advanced product candidates currently in Phase III clinical trials. Medarex is committed to building value by developing a diverse pipeline of antibody products to address the world's unmet healthcare needs. For more information about Medarex, visit its website at [www.medarex.com](http://www.medarex.com).

Public Relations  
Ono Pharmaceutical Co., Ltd.  
Tel: +81-6-6263-5670  
Fax: +81-6-6263-2950