



August 1, 2006

**Allowance of an investigational new drug application (IND) for ONO-4538 / MDX-1106,  
a fully human anti-PD-1 antibody**

Ono Pharmaceutical Co., Ltd. (HQ: Osaka, president: Toshiharu Korekane) and Medarex, Inc. (HQ: New Jersey, US, president and CEO: Donald L. Drakeman) announced today the allowance of an investigational new drug application (IND) filed by Medarex with the U.S. Food & Drug Administration (FDA) for ONO-4538/ MDX-1106, a fully human anti-PD-1 antibody which was created based on a collaboration agreement concluded with Medarex in May 2005 for the research and development of an anti-PD-1 antibody for the treatment of cancer.

With this allowance of an IND, Medarex will initiate a Phase I study of ONO-4538/ MDX-1106 in the US. This study is intended to evaluate the pharmacokinetics and the safety of ONO-4538/ MDX-1106 in patients with recurrent or treatment-refractory cancer.

PD-1 is one of the receptors expressed on the surface of activated lymphocytes, and is involved in the system of negative regulation for the suppression of activated lymphocytes. It has been reported that tumor cells and certain chronic viruses utilize this system to escape from host immune responses (which protect an individual from both harmful pathogens and tumors). It is anticipated that the blockade of the negative regulatory signal mediated by PD-1 will promote the host's immune response, in which tumor cells are recognized as foreign and eliminated. ONO-4538/ MDX-1106 has been shown to block this signaling pathway in order to potentially enhance the ability of the patient's immune system to attack the tumors and eliminate the viruses.

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“We believe that MDX-1106 / ONO-4538 is part of an emerging new class of immunopotentiators – antibodies that target immune regulatory pathways, such as CTLA-4- that are designed to boost a patient's immune response to eliminate cancer and chronic

infection,” said Dr. Donald L. Drakeman, president and CEO of Medarex. “We are pleased with the progress of our collaboration with Ono and look forward to developing MDX-1106 / ONO-4538 as an exciting new and potentially effective approach to fight cancer.”

“ONO-4538/ MDX-1106 is designed to suppress tumor growth through the use of the body’s own immune system in order to have an effect on cancers even which there currently are no effective treatments,” said Dr. Shozo Matsuoka, executive director of Development Headquarters at Ono. “Ono plans to promote the rapid development of this drug for patients all over the world in collaboration with Medarex.”

(Reference)

About Medarex

Medarex is a biopharmaceutical company focused on the discovery, development and potential commercialization of fully human antibody-based therapeutics to treat diseases including cancer, inflammation, autoimmune disorders and infectious diseases. Thirty-three of these therapeutic product candidates derived from Medarex technology are in human clinical testing or have had INDs submitted for such trials, with five of the most advanced product candidates currently in Phase III clinical trials. For more information about Medarex, visit its website at [www.medarex.com](http://www.medarex.com).

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