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Human Anti-human PD-1 Monoclonal Antibody "OPDIVO® Intravenous Infusion 20 mg/100 mg" Receives Manufacturing and Marketing Approval in Japan for the Treatment of Unresectable Melanoma

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; "ONO") announced that ONO has today received manufacturing and marketing approval for the human anti-human PD-1 monoclonal antibody "OPDIVO® Intravenous Infusion 20 mg/100 mg"("OPDIVO") for the treatment of unresectable melanoma.

Melanoma is considered to be a form of tumor characterized by the malignant transformation of pigment-producing cells located in the skin. In Japan, there has been an unmet need for an effective treatment for patients with surgically unresectable melanoma, who have an extremely poor prognosis that no treatment exists to significantly improve.

OPDIVO is a human anti-human PD-1 monoclonal antibody. PD-1 (programmed death-1), a receptor expressed on the surface of lymphocytes, plays a role in a regulatory pathway that suppresses activated lymphocytes in the body (negative signal). Available evidence suggests that cancer cells exploit this pathway to escape from immune responses. OPDIVO is thought to provide benefit by blocking PD-1-mediated negative regulation of lymphocytes (i.e., the interaction of PD-1 with its ligands PD-L1 and PD-L2), thereby enhancing the ability of the immune system to recognize cancer cells as foreign and eliminate them. OPDIVO is the world's first approved drug targeting PD-1.

"We are delighted to obtain a manufacturing and marketing approval as a drug targeting PD-1, which receives a lot of attention in tumor immunity, for the first time in the world." said Gyo Sagara, the President and Representative Director of ONO. "ONO would like to obtain approvals for additional indications on ongoing development for other cancers to bring many patients OPDIVO as soon as possible."

Accumulating further clinical data is important in ensuring that OPDIVO will be used more safely and effectively. ONO is committed to taking actions necessary for the proper use of OPDIVO by implementing a post-marketing use-results survey (all-case surveillance) and collecting clinical data on the safety and efficacy of OPDIVO pursuant to the conditions for its approval.

[About the pre-NHI reimbursement drug access program]

Currently, only dacarbazine, anticancer drug, monotherapy is available as standard drug therapy for the treatment of advanced melanoma in Japan. To help people who need early treatment with OPDIVO based on ethical considerations, ONO will provide access to OPDIVO free of charge as soon as it is ready. This program will be offered until the product is listed on the national health insurance (NHI) price list and at some limited medical institutions where Phase II clinical trials of OPDIVO were performed and those are prepared to accept the drug access program.

Product name	OPDIVO® Intravenous Infusion 20 mg/100 mg
Generic name (JAN)	Nivolumab (recombinant)
Indication	Unresectable melanoma
Dosage and administration	The recommended dose for adults is 2 mg/kg (body weight) of nivolumab administered as an intravenous infusion every 3 weeks.
Manufacturing and marketing approval date	July 4, 2014
Manufacturer/distributor	Ono Pharmaceutical Co., Ltd.
Conditions for approval	Because of the very limited number of patients treated with OPDIVO in Japanese clinical trials, ONO is required to perform a post-marketing use-results survey covering all cases until data on a certain minimum number of patients have been accumulated. Through these activities, ONO should identify the characteristics of patients to be treated with OPDIVO and collect safety and efficacy data as soon as possible, thereby taking actions necessary to ensure the proper use of OPDIVO.

About the agreement for OPDIVO®.

OPDIVO is a human anti-human PD-1 monoclonal antibody generated under a research collaboration entered into in May 2005 between ONO and the US-based company Medarex, Inc. When Medarex, Inc. was acquired by Bristol-Myers Squibb Company (“BMY”) in 2009, it also granted BMY its rights to develop and commercialize the human anti-human PD-1 monoclonal antibody in North America. Through the collaboration agreement entered into in September 2011 between ONO and BMY, ONO granted BMY exclusive rights to develop and commercialize OPDIVO in the rest of the world, except in Japan, Korea and Taiwan where ONO has retained all rights to develop and commercialize the compound.

About Ono Pharmaceutical Co., Ltd.

Ono Pharmaceutical Co., Ltd., headquartered in Osaka, Japan, is an R&D-oriented pharmaceutical company committed to creating innovative medicines in specific areas. It focuses especially on the diabetes and oncology areas. For more information, please visit ONO’s website at http://www.ono.co.jp./eng/index.html.