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ONO submits manufacturing approval partial amendment application for OPDIVO® (generic name: Nivolumab) for treatment of patients with unresectable melanoma in Japan

ONO PHARMACEUTICAL CO.,LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; "ONO") announced today that it has submitted manufacturing approval partial amendment application for the human anti-human PD-1 (programmed cell death-1) monoclonal antibody "OPDIVO® 20mg, 100mg Inj." (OPDIVO) for the "treatment of patients with unresectable melanoma" in Japan.

OPDIVO received the approval for the "treatment of patients with unresectable melanoma" in July 2014 in Japan, and this manufacturing approval partial amendment application aims to enable the use for the patients with untreated melanoma before chemotherapy.
Also, in addition to the current dosage and administration of "administering 2 mg/kg as an intravenous infusion over 60 minutes every 3 weeks", ONO also has submitted the additional application for the dosage and administration of "administering 3 mg/kg as an intravenous infusion over 60 minutes every 2 weeks".

Melanoma is considered to be a form of skin cancer characterized by the malignant transformation of pigment-producing cells located in the skin. Melanoma is high metastatic and the deadliest form of the disease.

OPDIVO is a human anti-human PD-1 monoclonal antibody. PD-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 as an immune checkpoint inhibitor.

OPDIVO is the first human anti-human PD-1 monoclonal antibody to receive regulatory approval for the treatment of patients with unresectable melanoma anywhere in the world in July 2014. ONO submitted an additional indication application for the treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer(NSCLC) (except non-squamous cell carcinoma) in April 2015, and for the treatment of patients with unresectable, advanced or recurrent NSCLC in July 2015 in Japan.
Also, the U.S. Food and Drug Administration (FDA) has approved OPDIVO for the treatment of patients with unresectable or metastatic melanoma and disease progression following Yervoy® (ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor in December 2014, and for the treatment of patients with metastatic squamous NSCLC with progression on or after platinum-based chemotherapy in March 2015.
Furthermore, the European Commission has approved OPDIVO for the treatment of advanced (unresectable or metastatic) melanoma in adults regardless of BRAF status in June 2015, and for the treatment of locally advanced or metastatic squamous NSCLC after prior chemotherapy in July 2015.

About the ONO PHARMACEUTICAL and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with ONO PHARMACEUTICAL, Bristol-Myers Squibb expanded its territorial rights to develop and commercialize OPDIVO globally except in Japan, South Korea and Taiwan, where ONO had retained all rights to the compound at the time. In July 2014, ONO and Bristol-Myers Squibb further expanded the companies' strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.