March 24, 2017

**ONO Receives Approval for OPDIVO® (Nivolumab) Intravenous Infusion for Treatment of Recurrent or Metastatic Head and Neck Cancer as a Partial Change in Approved Items of Manufacturing and Marketing Approval in Japan**

ONO PHARMACEUTICAL CO., LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; "ONO") and Bristol-Myers Squibb Company (NYSE: BMY) announced today that ONO received an approval for a partial change in approved items of the manufacturing and marketing approval of OPDIVO® Intravenous Infusion 20 mg and 100 mg ("Opdivo"), the human anti-human PD-1 (programmed cell death-1) monoclonal antibody, for the treatment of recurrent or metastatic head and neck cancer in Japan.

Head and neck cancer (HNC) is a general term describing malignant tumors occurring in the head and neck regions, such as the lip, oral cavity, nasal cavity, paranasal sinuses, epipharynx, oropharynx, hypopharynx, larynx, large salivary gland or mucosal melanoma. It is estimated that there are about 24,000 affected patients with HNC (excluding cancer of the thyroid gland) annually in Japan*[1]. Platinum-based chemotherapy has been recommended as first therapy for patients with recurrent or metastatic HNC. Most patients present with locoregionally advanced disease, and more than 50% have recurrence within 3 years*[2-4]. There have been no existing drugs which had demonstrated an extension of overall survival (OS) for patients with recurrent or metastatic HNC early after platinum therapy. Therefore, new treatment options are expected for this patient population.

Opdivo is the first treatment in the world to demonstrate an extension of OS compared to competitor drugs (Investigators' choice therapy) in those patients with HNC who recur or progress after platinum-based chemotherapy and are not eligible for local treatment. In addition, Opdivo demonstrated an improvement of quality of life compared to competitor drugs. Opdivo is the first immune checkpoint inhibitor approved for the treatment of HNC in Japan.

In the global Phase III clinical trial in HNC patients including Japanese patients (ONO-4538-11/ CA209141), Opdivo demonstrated statistically significant extension of OS, the primary endpoint, with a median OS of 7.49 months (95% confidence interval [CI]: 5.49 – 9.10), compared to 5.06 months (95% IC: 4.04 – 6.05) for the comparator arm (investigator's choice of therapy) , (hazard ratio [HR] = 0.70; 97.73% CI: 0.51 - 0.96; p=0.0101 [stratified log-rank test]). The safety profile of Opdivo in this study was consistent with that in prior studies, with no new safety signals identified.

ONO considers it to be important to accumulate further clinical data, in order to make sure that Opdivo can be used more properly and effectively. In accordance with the conditional approval, 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.

*[1]: Monitoring of Cancer Incidence in Japan (MCIJ 2012), National Cancer Center, Center for Cancer Control and Information Services

*[2]: Pignon JP, le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother Oncol 2009; 92:4-14.
*[3]: Bernier J, Domenge C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004; 350: 1945-52.
*[4]: Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamouscell carcinoma of the head and neck. N Engl J Med 2004; 350: 1937-44.

**Overview of OPDIVO® Intravenous Infusion 20 mg and 100 mg**

| | |
|---|---|
| Product name | OPDIVO® Intravenous Infusion 20 mg and 100 mg |
| Generic name (JAN) | Nivolumab (Genetical recombination) |
| Indication | • Unresectable melanoma<br>• Unresectable, advanced or recurrent non-small cell lung cancer<br>• Unresectable or metastatic renal cell carcinoma<br>• Relapsed or refractory classical Hodgkin lymphoma<br>• Recurrent or metastatic head and neck cancer |
| Dosage and administration | 1. Unresectable melanoma<br>Chemotherapy-naive patients:<br>Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks.<br>Chemotherapy-treated patients:<br>Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks or 2 mg/kg (body weight) of nivolumab every 3 weeks.<br>2. Unresectable, advanced or recurrent non-small cell lung cancer, unresectable or metastatic renal cell carcinoma, relapsed or refractory classical Hodgkin lymphoma and recurrent or metastatic head and neck cancer<br>Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks. |
| Manufacturer/distributor | Ono Pharmaceutical Co., Ltd. |
| Co-promotion | Bristol-Myers Squibb KK |
| Conditions for approval | 1. Risk Management Plan should be designed and appropriately implemented.<br>2. Because of the very limited number of patients treated with Opdivo in Japanese clinical trials, a post-marketing use-results survey covering all cases should be performed until data on a certain minimum number of patients have been accumulated. Through these activities, actions necessary to ensure the proper use of Opdivo should be taken by identifying the characteristics of patients to be treated with Opdivo and collecting safety and efficacy data as soon as possible. |

* Underlined parts show the revised ones due to the approval for the partial change in approved items of the manufacturing and marketing approval.

**Opdivo**

Opdivo is an immune checkpoint inhibitor that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2 to help restore anti-tumor immune response. In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in July 2014. Thereafter, Opdivo also received approval for additional indications of unresectable, advanced or recurrent non-small cell lung cancer in December 2015, unresectable or metastatic renal cell cancer in August 2016 and relapsed or refractory classical Hodgkin lymphoma in December 2016. In addition, ONO has submitted supplemental application for treatment of gastric cancer, and is conducting clinical development program including esophageal cancer, gastro-esophageal junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, malignant pleural mesothelioma, ovarian cancer, biliary tract cancer, etc.

Bristol-Myers Squibb (BMS) has a robust clinical development program in Opdivo monotherapy and in combination with other therapies in a variety of tumor types overseas. Opdivo has regulatory approval in more than 60 countries as part of the ONO - BMS collaboration.

In Japan, ONO and BMS (and BMS Japan subsidiary, BMSKK) have formed a strategic partnership that includes co-development, co-commercialization, and co-promotion of multiple immunotherapies for patients with cancer in Japan.

**About the ONO and BMS Collaboration**

In 2011, through a collaboration agreement with BMS, ONO granted BMS 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 BMS 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.

Contact
ONO PHARMACEUTICAL CO., LTD.
Corporate Communications
public_relations@ono.co.jp