

September 30, 2014

**Positive Phase 3 Data for Opdivo (nivolumab) in Advanced Melanoma Patients  
Previously Treated with Yervoy® (ipilimumab) Presented at the ESMO 2014 Congress**

**First Phase 3 Results Presented for a PD-1 Immune Checkpoint Inhibitor**

Bristol-Myers Squibb announced that the positive Phase 3 results for Opdivo (nivolumab) in advanced melanoma patients previously treated with Yervoy® (ipilimumab) was presented at ESMO 2014 Congress in Madrid on September 29(EST).

Opdivo is a human anti-human PD-1 monoclonal antibody generated under a research collaboration entered into in May 2005 between ONO PHARMACEUTICAL CO.,LTD. (“ONO”) and the US-based company Medarex, Inc. When Medarex, Inc. was acquired by Bristol-Myers Squibb Company (“BMS”) in 2009, it also granted BMS 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 BMS, ONO granted BMS exclusive rights to develop and commercialize Opdivo in the rest of the world, except in Japan, Korea and Taiwan where ONO had retained all rights to develop and commercialize the compound. On July 23, 2014, ONO and BMS signed a new collaboration agreement in which the companies agreed to jointly develop and commercialize Opdivo, ipilimumab and three early-stage immunotherapies in Japan, South Korea and Taiwan.

Furthermore, BMS has a robust clinical development program in a variety of tumor types overseas, including: Non-Small Cell Lung Cancer (NSCLC), Renal Cell Carcinoma (RCC), Melanoma, Head and Neck Cancer, Blood Cancer, Glioblastoma, Colorectal Cancer, Pancreatic Cancer, Gastric Cancer, Hepatocellular Carcinoma, Triple-Negative Breast Cancer, Small-Cell Cancer, Bladder Cancer. In Japan, ONO has launched it for melanoma treatment in September 2014. Also, ONO is conducting clinical development programs including RCC, NSCLC, Head and Neck Cancer, Gastric Cancer and esophageal cancer.

Please refer to the Press Release announced by BMS.

Contact

ONO PHARMACEUTICAL CO.,LTD.  
Corporate Communications  
public\_relations@ono.co.jp

Bristol-Myers Squibb K.K.  
Public Affairs & Communications  
03-6705-7013  
Keisuke Goto  
pac@bms.com



**Positive Phase 3 Data for *Opdivo* (nivolumab) in Advanced Melanoma Patients Previously Treated with *Yervoy* (ipilimumab) Presented at the ESMO 2014 Congress; First Phase 3 Results Presented for a PD-1 Immune Checkpoint Inhibitor**

- *Objective response rate was 32% in Opdivo treated patients and 11% in the reference arm of chemotherapy-treated patients*
- *Majority (95%) of responses were ongoing in Opdivo treated patients and median duration of response was not reached*
- *Overall frequency of adverse events was lower with Opdivo compared to chemotherapy; Opdivo treatment-related adverse events were managed using recommended treatment algorithms*

(PRINCETON, N.J., September 29, 2014) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) today announced positive results from CheckMate -037, a Phase 3 randomized, controlled open-label study of *Opdivo* (nivolumab), an investigational PD-1 immune checkpoint inhibitor, versus investigator’s choice chemotherapy (ICC) in patients with advanced melanoma who were previously treated with *Yervoy* (ipilimumab). Based on a planned interim analysis of the co-primary endpoint, the objective response rate (ORR) was 32% (95% CI = 24, 41) in the *Opdivo* arm (n=120) and 11% (95% CI = 4, 23) in the ICC reference arm (n=47) in patients with at least six months of follow up. The majority (95%) of responses were ongoing in the *Opdivo* arm and the median duration of response was not reached. ORR was based on RECIST criteria as evaluated by an independent radiologic review committee (IRRC). These data were highlighted at a ESMO 2014 Congress press briefing today in Madrid and will be presented during the Presidential Symposium at 4 p.m. CEST (Abstract #LBA3\_PR).

“These data are important as they mark the first presentation of results from a Phase 3 randomized study for the PD-1 immune checkpoint inhibitor class,” said Jeffrey S. Weber, MD, Ph.D., director of the Donald A. Adam Comprehensive Melanoma Research Center at Moffitt Cancer Center. “Additionally, the response rate and duration of response in patients treated with *Opdivo* are consistent with findings from the early Phase 1 trial in previously treated advanced melanoma (Study -003).”

Safety was reported on all patients treated in the *Opdivo* (n=268) and ICC (n=102) arms. The majority of *Opdivo* treatment-related adverse events (AEs) were Grade 1/2 and managed using recommended treatment algorithms. Grade 3/4 drug-related AEs were less frequent for the *Opdivo* arm (9% versus 31% of patients treated chemotherapy). Serious Grade 3/4 drug-related AEs were reported in 5% and 9% of patients treated with *Opdivo* and ICC, respectively. There was no Grade 3/4 pneumonitis

(inflammatory lung disease) with *Opdivo*. Discontinuations due to drug-related AEs, of any grade, occurred in 2% of *Opdivo*-treated patients and 8% of patients administered ICC. There were no deaths related to study drug toxicity.

“This second set of positive Phase 3 data for *Opdivo* in patients with advanced melanoma supports a deeper understanding of the potential of immuno-oncology in this disease,” said Michael Giordano, M.D., senior vice president, Head of Development, Oncology. “These results confirm our belief in the potential of immuno-oncology, and our broad development program continues to evaluate *Opdivo* in advanced melanoma across lines of therapy, both as a single agent and as part of a combination regimen.”

In June, Bristol-Myers Squibb announced that a randomized blinded comparative Phase 3 study evaluating *Opdivo* versus dacarbazine in patients with previously untreated BRAF wild-type advanced melanoma (CheckMate -066) was stopped early because an analysis conducted by the independent Data Monitoring Committee showed evidence of superior overall survival in patients receiving *Opdivo* compared to the control arm. The Company is working with investigators on the future presentation and publication of the results from CheckMate -066.

Bristol-Myers Squibb has proposed the name *Opdivo* (pronounced op-dee-voh), which, if approved by health authorities, will serve as the trademark for nivolumab.

### **About CheckMate 037**

CheckMate -037 is a Phase 3 randomized, open-label study (n=370) designed to estimate the ORR in the *Opdivo* arm and compare the OS of patients treated with *Opdivo* versus those patients administered ICC. Patients in the trial were randomized 2:1 to receive *Opdivo* 3 mg/kg by intravenous infusion every two weeks (n=268) or ICC (dacarbazine 1000 mg/m<sup>2</sup> every three weeks or carboplatin AUC 6 plus paclitaxel 175 mg/m<sup>2</sup> every three weeks; n=102) until progression or unacceptable toxicity. Patients were classified by PD-1 ligand expression, BRAF status (wild type or mutated) and best response to prior treatment with *Yervoy*. Co-primary endpoints of the study are ORR and overall survival (OS). Response, as measured by standard RECIST 1.1 criteria by an IRRC, was assessed nine weeks after randomization, every six weeks for the first 12 months and then every 12 weeks. An interim analysis of OS had not taken place at the time of the ORR analysis.

### **About Opdivo**

Cancer cells may exploit “regulatory” pathways, such as checkpoint pathways, to hide from the immune system and shield the tumor from immune attack. *Opdivo* is an investigational, fully-human

PD-1 immune checkpoint inhibitor that binds to the checkpoint receptor PD-1 (programmed death-1) expressed on activated T-cells.

Bristol-Myers Squibb has a broad, global development program to study *Opdivo* in multiple tumor types consisting of more than 35 trials – as monotherapy or in combination with other therapies – in which more than 7,000 patients have been enrolled worldwide. Among these are several potentially registrational trials in non-small cell lung cancer (NSCLC), melanoma, renal cell carcinoma (RCC), head and neck cancer, glioblastoma and non-Hodgkin lymphoma.

In 2013, the FDA granted Fast Track designation for *Opdivo* (nivolumab) in NSCLC, melanoma and RCC. In April 2014, the company initiated a rolling submission with the FDA for *Opdivo* in third-line pre-treated squamous cell NSCLC and expects to complete the submission by year-end. The FDA granted *Opdivo* Breakthrough Therapy Designation in May 2014 for the treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant and brentuximab. On July 4, ONO PHARMACEUTICAL CO. announced that *Opdivo* received manufacturing and marketing approval in Japan for the treatment of patients with unresectable melanoma, making *Opdivo* the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world. On September 26, Bristol-Myers Squibb announced that the FDA accepted for priority review the BLA for previously treated advanced melanoma, and the Prescription Drug User Fee Act (PDUFA) goal date for a decision is March 30, 2015. The FDA also granted *Opdivo* Breakthrough Therapy status for this indication. In the European Union, the European Medicines Agency (EMA) has validated for review the Marketing Authorization Application (MAA) for *Opdivo* in advanced melanoma. The application has also been granted accelerated assessment by the EMA's Committee for Medicinal Products for Human Use (CHMP).

### **About Advanced Melanoma**

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin. Metastatic melanoma is the deadliest form of the disease, and occurs when cancer spreads beyond the surface of the skin to the other organs, such as the lymph nodes, lungs, brain or other areas of the body. The incidence of melanoma has been increasing for at least 30 years. In 2012, an estimated 232,130 melanoma cases<sup>※</sup> were diagnosed globally. Melanoma is mostly curable when treated in its early stages. However, in its late stages, the average survival rate has historically been just six months with a one-year mortality rate of 75 percent, making it one of the most aggressive forms of cancer.

## **Immuno-Oncology at Bristol-Myers Squibb**

Surgery, radiation, cytotoxic or targeted therapies have represented the mainstay of cancer treatment over the last several decades, but long-term survival and a positive quality of life have remained elusive for many patients with advanced disease.

To address this unmet medical need, Bristol-Myers Squibb is leading advances in the innovative field of immuno-oncology, which involves agents whose primary mechanism is to work directly with the body's immune system to fight cancer. The company is exploring a variety of compounds and immunotherapeutic approaches for patients with different types of cancer, including researching the potential of combining immuno-oncology agents that target different and complementary pathways in the treatment of cancer.

Bristol-Myers Squibb is committed to advancing the science of immuno-oncology, with the goal of changing survival expectations and the way patients live with cancer.

## **About the Bristol-Myers Squibb and ONO PHARMACEUTICAL 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. On July 23, 2014, Bristol-Myers Squibb and ONO PHARMACEUTICAL 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.

## **About Bristol-Myers Squibb**

Bristol-Myers Squibb is a global pharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit [www.bms.com](http://www.bms.com), or follow us on Twitter at <http://twitter.com/bmsnews>.

## **Bristol-Myers Squibb Forward-Looking Statement**

*This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of*

*them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that Opdivo will receive regulatory approval in the U.S. or, if approved, that it will become a commercially successful product. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2013 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.*