November 19, 2014

Study Comparing *Opdivo* (nivolumab) to Chemotherapy in Treatment Naïve Advanced Melanoma Patients Marks First PD-1 Immune Checkpoint Inhibitor to Demonstrate a Survival Benefit in a Phase 3 Trial

(PRINCETON, NJ, November 16, 2014) – Bristol-Myers Squibb Company (NYSE: BMY) today announced results from CheckMate -066, a Phase 3 randomized double blind study, comparing *Opdivo* (nivolumab), an investigational PD-1 immune checkpoint inhibitor, to the chemotherapy dacarbazine (DTIC) in patients with treatment naïve BRAF wild-type advanced melanoma (n=418).

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 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.

Late in September, FDA accepted for priority review the Biologics License Application for previously treated advanced melanoma based on data from first Phase 3 randomized trial of Opdivo. Agency granted second breakthrough therapy designation for Opdivo. European Medicines Agency validated the Marketing Authorization Application for advanced melanoma. Accelerated assessment has also been granted for this application. Also EMA validated for review the Marketing Authorization Application (MAA) for Opdivo in non-small cell lung cancer (NSCLC).

Furthermore, BMS has a robust clinical development program in a variety of tumor types overseas, including: 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 Lung 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.

Attached from the following page is the press release made by BMS for your information.

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

Study Comparing *Opdivo* (nivolumab) to Chemotherapy in Treatment Naïve Advanced Melanoma Patients Marks First PD-1 Immune Checkpoint Inhibitor to Demonstrate a Survival Benefit in a Phase 3 Trial

- ***Opdivo demonstrated superior overall survival vs. dacarbazine with a one-year survival rate of 73% vs.42% and a 58% decrease in the risk of death (Hazard Ratio [HR] = 0.42, P<0.0001)***
- ***Objective response rate was significantly higher for Opdivo than dacarbazine (40% vs.14%), including a higher percentage of complete responses (7.6% vs. 1%)***
- ***Safety and tolerability were well characterized with fewer treatment-related Grade 3/4 adverse events observed with Opdivo than dacarbazine (11.7% vs. 17.6%)***

(PRINCETON, NJ, November 16, 2014) **–** Bristol-Myers Squibb Company (NYSE: BMY) today announced results from CheckMate -066, a Phase 3 randomized double blind study, comparing *Opdivo* (nivolumab), an investigational PD-1 immune checkpoint inhibitor, to the chemotherapy dacarbazine (DTIC) in patients with treatment naïve BRAF wild-type advanced melanoma (n=418). The study met the primary endpoint of overall survival (OS) with the median OS not reached for *Opdivo* vs. 10.8 months for DTIC. The one-year survival rate was 73% for *Opdivo* vs. 42% for DTIC and there was a 58% decrease in the risk of death for patients treated with *Opdivo* (Hazard Ratio for death [HR]: 0.42, P<0.0001). This survival advantage was also observed in *Opdivo*-treated patients in both PD-L1 positive and PD-L1 negative patients. Findings from CheckMate -066 were published today in *The New England Journal of Medicine* and presented during an oral session at the Society for Melanoma Research 2014 International Congress in Zurich, Switzerland.

“The results from CheckMate -066 are significant as they represent the first time a PD-1 immune checkpoint inhibitor has shown a survival benefit in a randomized Phase 3 trial,” said Prof Caroline Robert, Professor of Dermatology, Head of the Dermatology Unit, Institute Gustave Roussy and lead author of the *New England Journal of Medicine* manuscript. “This represents a major milestone in the study of treatment naïve patients with wild-type BRAF advanced melanoma.”

Safety was reported in all patients treated in the *Opdivo* and DTIC arms. Fewer discontinuations were observed with *Opdivo* than DTIC (6.8% vs. 11.7%) as well as for treatment-related Grade 3/4 adverse events (AEs) (11.7% vs. 17.6%), which were managed using established safety algorithms. The most common *Opdivo* treatment-related AEs were fatigue (20%), pruritus (17%), and nausea (16.5%).

Common adverse events in the DTIC arm were consistent with those in previous reports and included nausea (41.5%), vomiting (21%), fatigue (15%), diarrhea (15%) and hematological toxicities. No deaths were attributed to study drug toxicity in either arm.

"Treatment naïve advanced melanoma patients who received nivolumab in this study had clinically important improvements in both overall survival and objective response rates compared to DTIC," said Georgina V. Long, M.D., Ph.D., Melanoma Institute Australia & the University of Sydney and Mater Hospital and presenter of the results. "This study also confirms our hypothesis on the role of PD-L1 expression in advanced melanoma. In CheckMate -066, both PD-L1 positive and negative patients treated with nivolumab had a clear survival benefit."

"Results from this Phase 3 *Opdivo* trial with a survival endpoint build upon the pioneering science that led to the introduction of *Yervoy* in 2011 and underscore our strategic commitment to provide more patients with the potential opportunity for long-term survival," said Michael Giordano, senior vice president, Head of Development, Oncology, Bristol-Myers Squibb. "And, we continue to develop our immuno-oncology portfolio across the continuum of melanoma and multiple other cancers as single agents and as part of combination regimens."

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 the CheckMate -066 Trial Design

CheckMate -066 is a Phase 3 randomized, double-blind study of patients with treatment naïve BRAF wild-type unresectable Stage III and IV melanoma. The trial enrolled 418 patients who were randomized to receive either *Opdivo* 3 mg/kg every two weeks (n=210) or DTIC 1000 mg/m2 every three weeks (n=208). Treatment continued until there was disease progression or an unacceptable level of toxicity. Thirty-eight percent of patients in the DTIC arm received *Yervoy* (ipilimumab) after stopping study treatment. All randomized patients were followed for up to 16.7 months at the time of database lock. The primary endpoint was OS. Secondary endpoints included progression free survival (PFS), objective response rate (ORR) by RECIST v1.1 criteria and PD-L1 expression as a predictive biomarker of OS. PD-L1 positivity was defined as at least 5% of tumor cells showing cell-surface PD-L1 staining. The study, which was designed in consultation with the Committee for Medicinal Products for Human Use (CHMP), was primarily conducted in countries where DTIC is a commonly-used treatment in the first-line setting, including Canada, Europe and Australia, but not at U.S. trial sites. On June 24, 2014, Bristol-Myers Squibb announced that CheckMate -066 was stopped early because an analysis conducted by the independent Data Monitoring Committee showed evidence of superior OS in patients receiving

Opdivo compared to the control arm, DTIC. As a result, patients in the trial were unblinded and allowed to receive *Opdivo*. However, the results reported today are from the double-blind portion of the study before the amendment.

Detailed Study Results

Median OS was not reached for patients treated with *Opdivo* and was 10.8 months for DTIC (95% CI 9.3–12.1). The one-year survival rate was 73% for *Opdivo* (95% CI = 66-79) vs. 42% for DTIC (95% CI = 33-51). There was a 58% decrease in the risk of death for patients treated with *Opdivo* (Hazard Ratio for death [HR]: 0.42; 99.79% CI = 0.25-0.73; P<0.0001). Median PFS was 5.1 months and 2.2 months, respectively (HR: 0.43; 95% CI = 0.34–0.56; P < 0.0001).

ORR was also significantly higher for *Opdivo* than DTIC (40% vs. 14%, p<0.0001). Complete responses were observed in 7.6% of *Opdivo*-treated patients vs. 1% for DTIC. Median duration of response was not reached for *Opdivo* responders and was six months for DTIC (95% CI, 3.0–not estimable). Responses were ongoing in 86% of *Opdivo* responders compared to 51% for DTIC responders.

In both the PD-L1 positive and PD-L1 negative/indeterminate subgroups, *Opdivo*-treated patients had improved OS vs. DTIC (unstratified HR 0.30, 95% CI, 0.15-0.60 in PD-L1 positive patients; 0.48, 95% CI 0.32-0.71 in PD-L1 negative/indeterminate patients). Median OS was not reached in either PD-L1 subgroup in the *Opdivo* arm. In the DTIC arm, mOS was slightly longer in the PD-L1 positive subgroup (12 vs. 10 months).

Safety was reported in all patients treated in the *Opdivo* and DTIC arms. The incidence of any-grade treatment-related AEs was similar between the *Opdivo* and DTIC groups (74.3% and 75.6%, respectively). However, fewer treatment-related Grade 3/4 AEs were observed with *Opdivo* than DTIC (11.7% vs. 17.6%), which were managed using established safety algorithms, and there were fewer treatment discontinuations (6.8% vs. 11.7%). The frequency of Grade 3/4 treatment-related serious AEs was similar between the *Opdivo* and DTIC group (5.8% and 5.9%, respectively). The most common *Opdivo* treatment-related AEs were fatigue (20%), pruritus (17%), and nausea (16.5%). Common AEs in the DTIC arm were consistent with those in previous reports and included nausea (41.5%), vomiting (21%), fatigue (15%), diarrhea (15%) and hematological toxicities. No deaths were attributed to study drug toxicity in either arm.

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 50 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 2012, the FDA granted Fast Track designation for *Opdivo* 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 and on September 2 announced the launch. Thereby *Opdivo* became the first PD-1 immune checkpoint inhibitor which was approved and launched in the world. On September 26, Bristol-Myers Squibb announced that the FDA accepted for priority review the Biologics License Application for previously treated advanced melanoma, and the Prescription Drug User Fee Act 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 for *Opdivo* in advanced melanoma. The application has also been granted accelerated assessment by the EMA's CHMP. The EMA also validated for review the MAA for nivolumab in NSCLC.

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 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 CO., 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 CO 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, 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.