June 3rd, 2013

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Fully Human Anti-PD-1 Antibody "ONO-4538/BMS-936558"
Results from Phase 1 Study in Patients with Melanoma Presented
at Annual Meeting of the American Society of Clinical Oncology (ASCO)

Bristol-Myers Squibb Company (hereinafter referred to as "BMY") announced the results from Phase 1 combination study with Yervoy® (ipilimumab) in patients with melanoma was presented at 49th annual meeting of the American Society of Clinical Oncology (ASCO), on June 2nd (US time).

ONO-4538/BMS-936558, a fully human anti-PD-1 antibody, is an investigational cancer immunotherapy generated under a research collaboration entered into in May 2005 between Ono Pharmaceutical Co., Ltd. (hereinafter referred to as "Ono") and Medarex, Inc. When Medarex, Inc. was acquired by BMY in 2009, it also granted BMY its rights to develop and commercialize the anti-PD-1 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 ONO-4538/BMS-936558 in the rest of the world, except in Japan, Korea and Taiwan where Ono has retained all rights to develop and commercialize the compound.

BMY is conducting a Phase 3 studies in NSCLC, RCC and melanoma in the overseas countries where BMY has the rights to develop and commercialize the compound. On the other hand, in Japan, Ono is conducting Phase 2 studies in NSCLC and melanoma, and a global Phase 3 study in RCC.

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

Bristol-Myers Squibb

Bristol-Myers Squibb Announces Phase 1 Results from First Trial Combining Immune Checkpoint Inhibitors, Investigational Agent Nivolumab and Yervoy® (ipilimumab), in Patients with Advanced Melanoma

- ***53% response rate observed in patients receiving 1 mg/kg nivolumab plus 3 mg/kg Yervoy concurrently (n=9 of 17), the dose used in the Phase 3 trial; of these responders all experienced at least 80% tumor shrinkage within 12 weeks***
- ***Grade 3-4 treatment-related adverse events occurred in 53% of patients on the concurrent-regimen and 18% of patients on the sequenced-regimen***
- ***Data published today in New England Journal of Medicine***
- ***Estimated survival data from this Phase 1 trial presented at 49th annual meeting of the American Society of Clinical Oncology***
- ***Phase 3 trial of nivolumab in combination with Yervoy in advanced melanoma underway***

(PRINCETON, NJ, June 2, 2013) – Bristol-Myers Squibb Company (NYSE: BMY) today announced results from Study 004, a dose-ranging Phase 1 trial (n=86) evaluating the safety and anti-tumor activity of its investigational PD-1 receptor blocker, nivolumab, combined either concurrently (n=53) or sequentially (n=33) with *Yervoy*® (ipilimumab) in patients with advanced melanoma. In patients who received the dose used in the Phase 3 trial (1 mg/kg nivolumab + 3 mg/kg *Yervoy*) in the concurrent regimen, 53% (n=9 of 17) had confirmed objective responses (OR) by mWHO criteria. In all nine of these responders, tumors shrank by at least 80% by the time of the first scheduled clinical treatment assessment (12 weeks), including three complete responses (CRs). In response-evaluable patients across all concurrent cohorts, 40% (n=21 of 52) had an OR. Sixteen patients (31%) had tumor shrinkage of at least 80% by the time of the first clinical trial assessment, including five CRs. Responses were ongoing among 19 of 21 responders, with responses lasting from between 6.1+ to 72.1+ weeks at the time of data analysis. Clinical activity was observed in both the concurrent and sequenced regimens. Median overall survival has not been reached after approximately 13 months of median follow up in the concurrent cohorts. The estimated one-year survival rate across all concurrent cohorts was 82% (95% CI 69.0 – 94.4%).

Grade 3-4 treatment-related adverse events occurred in 53% of patients on the concurrent-regimen and 18% of patients on the sequenced-regimen. No treatment-related deaths were reported.

The data on nivolumab in combination with *Yervoy* were published today in the *New England Journal of Medicine* (NEJM). The estimated survival data were presented at the 49th Annual Meeting of the American Society of Clinical Oncology (Abstract # 9012).

"This is the first clinical trial to evaluate the safety and efficacy of combining two immune-checkpoint inhibitors, which are agents that target the pathways tumor cells use to evade recognition and destruction by the immune system," said Dr. Jedd D. Wolchok, Ludwig Center for Cancer Immunotherapy at Memorial Sloan-Kettering Cancer Center, presenter of the results and lead author on the *New England Journal of Medicine* paper. "The responses observed with the concurrent combination of nivolumab and ipilimumab in this Phase 1 trial of patients with advanced melanoma are very encouraging and support further research in randomized trials to evaluate the concept of combining agents that target different, but complementary, immune checkpoint pathways."

"An unmet medical need remains for many types of advanced cancer and Bristol-Myers Squibb is committed to leading advances in a new field of research, immuno-oncology, which is a rapidly evolving, innovative treatment modality centered on harnessing the natural capabilities of a patient's own immune system to fight cancer," said Brian Daniels, senior vice president, Global Development and Medical Affairs, Bristol-Myers Squibb. "Results from this Phase 1 study provide important insights about the potential of combinations in immuno-oncology and deepen our understanding of how cancer cells evade the immune system."

Bristol-Myers Squibb is developing a robust pipeline of compounds that directly modulate the immune system across a broad range of cancers. This includes the development program for nivolumab, which now consists of seven potentially registrational trials in three tumor types: non-small cell lung cancer (NSCLC), advanced renal cell carcinoma and advanced melanoma, including one in combination with *Yervoy*. The Phase 3 development program for *Yervoy* is also ongoing and includes Phase 3 trials in adjuvant melanoma, NSCLC and metastatic castrate-resistant prostate cancer.

Study 004 Results

Clinical activity was observed in both the concurrent and sequenced regimens. In the concurrent-regimen cohort, confirmed OR by mWHO criteria was observed in nine of 17 (53%) patients treated at a dose of 1 mg/kg nivolumab + 3 mg/kg *Yervoy*, the dose used in the Phase 3 trial. All nine responders achieved 80% or greater tumor reduction by the time of the first scheduled clinical trial assessment (12 weeks), including three CRs. In response-evaluable patients across all concurrent cohorts, OR was observed in 21 of 52 (40%) of patients. Sixteen patients (31%) had tumor shrinkage of at least 80% by the time of the first clinical trial assessment (12 weeks). Four patients experienced an OR by immune-related response criteria and two patients had unconfirmed responses. These six patients were not included in the calculation of objective response rates. Responses were ongoing among 19 of 21 responders, with responses lasting from between 6.1+ to 72.1+ weeks at the time of

data analysis. The median overall survival has not been reached after approximately 13 months of median follow up in the combined concurrent cohorts. The estimated one-year survival rate across all concurrent cohorts was 82% (95% CI 69.0 – 94.4%).

In the sequenced-regimen cohorts, six of 30 patients achieved OR (20%) including one CR. Four (13%) patients achieved 80% or greater tumor reduction at 8 weeks. Three patients had immune-related responses and three patients had unconfirmed responses. These six patients were not included in the calculation of objective response rates. These findings showed that patients who did not respond to prior *Yervoy* responded to subsequent nivolumab.

AEs were more frequent in patients treated with the concurrent combination compared to each single agent. No treatment-related deaths were reported. In the concurrent-regimen, treatment-related AEs occurred in 93% of patients with the most common being rash (55%), pruritus (47%), fatigue (38%), and diarrhea (34%). Grade 3-4 treatment-related AEs were observed in 53% of patients, the most common being elevations in lipase (13%), aspartate aminotransferase (13%) and alanine aminotransferase (11%). Three patients had Grade 1-2 pneumonitis (6%) and one patient had Grade 3 pneumonitis (2%). In the sequenced regimen, treatment-related AEs occurred in 73% of patients with the most common being pruritus (18%) and lipase elevation (12%). Grade 3-4 treatment-related AEs were observed in 18% of patients with lipase elevation (6%) as the most common. One patient had Grade 1-2 pneumonitis (3%).

About Study 004

Study 004 is a dose-ranging Phase 1 study (n=86) evaluating the safety, antitumor activity and pharmacokinetics of nivolumab in concurrent and sequenced combination with *Yervoy* in patients with advanced melanoma.

The study consists of two treatment regimens, both of which are administered as intravenous infusions. In the concurrent regimen (n=53), eligible patients received nivolumab and *Yervoy* every 3 weeks for 4 doses, followed by nivolumab alone every 3 weeks for 4 doses. Combined treatment was subsequently continued every 12 weeks for up to 8 doses. Cohorts of a maximum of seventeen patients per dose level (0.3 mg/kg nivolumab + 3 mg/kg *Yervoy*; 1 mg/kg nivolumab + 3 mg/kg *Yervoy*; 3 mg/kg nivolumab + 1 mg/kg *Yervoy*; 3 mg/kg nivolumab + 3 mg/kg *Yervoy*) were enrolled. In the sequenced regimen (n=33), patients previously treated with *Yervoy* received nivolumab alone every 2 weeks. Cohorts of six patients per dose level (1, 3 mg/kg) were enrolled. After completion of therapy, patients without confirmed disease progression were followed for ≤2.5 years. Patients with initial disease control and subsequent disease progression could be retreated with the original regimen. Initial

disease control was defined as complete response, partial response, or stable disease for ≥24 weeks. All cohorts were enrolled in sequence from each other.

Two Distinct Immune Checkpoint Inhibitors

Nivolumab and *Yervoy* are both immune checkpoint inhibitors, but they are monoclonal antibodies that target different receptors for distinct T-cell checkpoint pathways.

Nivolumab is an investigational, fully-human IgG4 anti-PD-1 receptor blocking monoclonal antibody that binds to the checkpoint receptor PD-1 (programmed death-1) expressed on activated T cells. Nivolumab inhibits the binding of PD-1 with its tumor-expressed ligands, programmed death-ligand 1 (PD-L1/B7-H1) and PD-L2 (B7-DC). Blocking of the interaction of the PD-1 receptor with its ligands may allow T-cells to elicit an anti-tumor immune response.

Yervoy, which is a recombinant, human monoclonal antibody, blocks the cytotoxic T-lymphocyte antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Ipilimumab binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation. The mechanism of action of ipilimumab's effect in patients with melanoma is indirect through T-cell mediated anti-tumor immune responses. On March 25, 2011, the FDA approved *Yervoy* 3 mg/kg monotherapy for patients with unresectable or metastatic melanoma. *Yervoy* is now approved in 41 countries.

Important Safety Information

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests (LFTs) and thyroid function tests at baseline and before each dose.

Permanently discontinue YERVOY for any of the following:

- Persistent moderate adverse reactions or inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day
- Failure to complete full treatment course within 16 weeks from administration of first dose
- Severe or life-threatening adverse reactions, including any of the following
    - Colitis with abdominal pain, fever, ileus, or peritoneal signs; increase in stool frequency (≥7 over baseline), stool incontinence, need for intravenous hydration for >24 hours, gastrointestinal hemorrhage, and gastrointestinal perforation
    - AST or ALT >5 × the upper limit of normal (ULN) or total bilirubin >3 × the ULN
    - Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full-thickness dermal ulceration or necrotic, bullous, or hemorrhagic manifestations
    - Severe motor or sensory neuropathy, Guillain-Barré syndrome, or myasthenia gravis
    - Severe immune-mediated reactions involving any organ system
    - Immune-mediated ocular disease which is unresponsive to topical immunosuppressive therapy

Immune-mediated Enterocolitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening or fatal (diarrhea of ≥7 stools above baseline, fever, ileus, peritoneal signs; Grade 3-5) immune-mediated enterocolitis occurred in 34 (7%) and moderate (diarrhea with up to 6 stools above baseline, abdominal pain, mucus or blood in stool; Grade 2) enterocolitis occurred in 28 (5%) patients
- Across all YERVOY-treated patients (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis
- Infliximab was administered to 5 of 62 (8%) patients with moderate, severe, or life-threatening immune-mediated enterocolitis following inadequate response to corticosteroids
- Monitor patients for signs and symptoms of enterocolitis (such as diarrhea, abdominal pain, mucus or blood in stool, with or without fever) and of bowel perforation (such as peritoneal signs and ileus). In symptomatic patients, rule out infectious etiologies and consider endoscopic evaluation for persistent or severe symptoms

- Permanently discontinue YERVOY in patients with severe enterocolitis and initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue over at least 1 month. In clinical trials, rapid corticosteroid tapering resulted in recurrence or worsening symptoms of enterocolitis in some patients
- Withhold YERVOY for moderate enterocolitis; administer anti-diarrheal treatment and, if persistent for >1 week, initiate systemic corticosteroids (0.5 mg/kg/day prednisone or equivalent)

Immune-mediated Hepatitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening, or fatal hepatotoxicity (AST or ALT elevations >5x the ULN or total bilirubin elevations >3x the ULN; Grade 3–5) occurred in 8 (2%) patients, with fatal hepatic failure in 0.2% and hospitalization in 0.4%
- 13 (2.5%) additional YERVOY-treated patients experienced moderate hepatotoxicity manifested by LFT abnormalities (AST or ALT elevations >2.5x but ≤5x the ULN or total bilirubin elevation >1.5x but ≤3x the ULN; Grade 2)
- Monitor LFTs (hepatic transaminase and bilirubin levels) and assess patients for signs and symptoms of hepatotoxicity before each dose of YERVOY. In patients with hepatotoxicity, rule out infectious or malignant causes and increase frequency of LFT monitoring until resolution
- Permanently discontinue YERVOY in patients with Grade 3-5 hepatotoxicity and administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When LFTs show sustained improvement or return to baseline, initiate corticosteroid tapering and continue over 1 month. Across the clinical development program for YERVOY, mycophenolate treatment has been administered in patients with persistent severe hepatitis despite high-dose corticosteroids
- Withhold YERVOY in patients with Grade 2 hepatotoxicity

Immune-mediated Dermatitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening or fatal immune-mediated dermatitis (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, or

rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations; Grade 3–5) occurred in 13 (2.5%) patients

  - 1 (0.2%) patient died as a result of toxic epidermal necrolysis
  - 1 additional patient required hospitalization for severe dermatitis

- There were 63 (12%) YERVOY-treated patients with moderate (Grade 2) dermatitis
- Monitor patients for signs and symptoms of dermatitis such as rash and pruritus. Unless an alternate etiology has been identified, signs or symptoms of dermatitis should be considered immune-mediated
- Permanently discontinue YERVOY in patients with severe, life-threatening, or fatal immune-mediated dermatitis (Grade 3-5). Administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When dermatitis is controlled, corticosteroid tapering should occur over a period of at least 1 month. Withhold YERVOY in patients with moderate to severe signs and symptoms
- Treat mild to moderate dermatitis (e.g., localized rash and pruritus) symptomatically. Administer topical or systemic corticosteroids if there is no improvement within 1 week

Immune-mediated Neuropathies:

- In the pivotal Phase 3 study in YERVOY-treated patients, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported
- Across the clinical development program of YERVOY, myasthenia gravis and additional cases of Guillain-Barré syndrome have been reported
- Monitor for symptoms of motor or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, or paresthesia. Permanently discontinue YERVOY in patients with severe neuropathy (interfering with daily activities) such as Guillain-Barré–like syndromes
- Institute medical intervention as appropriate for management of severe neuropathy. Consider initiation of systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe neuropathies. Withhold YERVOY in patients with moderate neuropathy (not interfering with daily activities)

Immune-mediated Endocrinopathies:

- In the pivotal Phase 3 study in YERVOY- treated patients, severe to life-threatening immune-mediated endocrinopathies (requiring hospitalization, urgent medical intervention, or interfering with activities of daily living; Grade 3-4) occurred in 9 (1.8%) patients
    - All 9 patients had hypopituitarism, and some had additional concomitant endocrinopathies such as adrenal insufficiency, hypogonadism, and hypothyroidism.
    - 6 of the 9 patients were hospitalized for severe endocrinopathies
- Moderate endocrinopathy (requiring hormone replacement or medical intervention; Grade 2) occurred in 12 (2.3%) YERVOY-treated patients and consisted of hypothyroidism, adrenal insufficiency, hypopituitarism, and 1 case each of hyperthyroidism and Cushing's syndrome
- Median time to onset of moderate to severe immune-mediated endocrinopathy was 11 weeks and ranged up to 19.3 weeks after the initiation of YERVOY
- Monitor patients for clinical signs and symptoms of hypophysitis, adrenal insufficiency (including adrenal crisis), and hyper- or hypothyroidism
    - Patients may present with fatigue, headache, mental status changes, abdominal pain, unusual bowel habits, and hypotension, or nonspecific symptoms which may resemble other causes such as brain metastasis or underlying disease. Unless an alternate etiology has been identified, signs or symptoms should be considered immune-mediated
    - Monitor thyroid function tests and clinical chemistries at the start of treatment, before each dose, and as clinically indicated based on symptoms. In a limited number of patients, hypophysitis was diagnosed by imaging studies through enlargement of the pituitary gland
- Withhold YERVOY in symptomatic patients. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) and initiate appropriate hormone replacement therapy. Long-term hormone replacement therapy may be necessary

Other Immune-mediated Adverse Reactions, Including Ocular Manifestations:

- In the pivotal Phase 3 study in YERVOY-treated patients, clinically significant immune-mediated adverse reactions seen in <1% were: nephritis, pneumonitis, meningitis, pericarditis, uveitis, iritis, and hemolytic anemia
- Across the clinical development program for YERVOY, immune-mediated adverse reactions also reported with <1% incidence were: myocarditis, angiopathy, temporal arteritis, vasculitis,

polymyalgia rheumatica, conjunctivitis, blepharitis, episcleritis, scleritis, leukocytoclastic vasculitis, erythema multiforme, psoriasis, pancreatitis, arthritis, and autoimmune thyroiditis

- Permanently discontinue YERVOY for clinically significant or severe immune-mediated adverse reactions. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe immune-mediated adverse reactions
- Administer corticosteroid eye drops for uveitis, iritis, or episcleritis. Permanently discontinue YERVOY for immune-mediated ocular disease unresponsive to local immunosuppressive therapy

Pregnancy & Nursing:

- YERVOY is classified as pregnancy category C. There are no adequate and well-controlled studies of YERVOY in pregnant women. Use YERVOY during pregnancy only if the potential benefit justifies the potential risk to the fetus
- Human IgG1 is known to cross the placental barrier and YERVOY is an IgG1; therefore, YERVOY has the potential to be transmitted from the mother to the developing fetus
- It is not known whether YERVOY is secreted in human milk. Because many drugs are secreted in human milk and because of the potential for serious adverse reactions in nursing infants from YERVOY, a decision should be made whether to discontinue nursing or to discontinue YERVOY

Common Adverse Reactions:

- The most common adverse reactions (≥5%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%)

Please see full Prescribing Information, including **Boxed WARNING regarding immune-mediated adverse reactions available at packageinserts.bms.com/yervoy.**

About the Bristol-Myers Squibb and Ono Pharmaceutical Partnership

Through a collaboration agreement with Ono Pharmaceutical in 2011, Bristol-Myers Squibb expanded its territorial rights to develop and commercialize nivolumab (BMS-936558/ONO-4538) globally except in Japan, Korea and Taiwan where Ono has retained all rights to the compound.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please 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 product development. 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 the late-stage clinical trials described in this release will support regulatory filings, that nivolumab will receive regulatory approval, that the combination use of nivolumab and Yervoy will receive regulatory approval, or that, if approved, they will become commercially successful. 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, 2012, 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.

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