Multiple Bristol-Myers Squibb Oncology Compounds to be Featured in Oral Presentations at 56th Annual American Society for Hematology (ASH) Meeting

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- Study results from investigational agents Opdivo (nivolumab), elotuzumab, and ulocuplumab, as well as Sprycel (dasatinib), will be highlighted
- First presentation of data for Opdivo in Hodgkin lymphoma and non-Hodgkin lymphoma, and final Phase 2 results of elotuzumab in multiple myeloma highlight potential of immuno-oncology in hematologic malignancies
- Breadth of program demonstrates company’s growing commitment to the field of hematology through immuno-oncology leadership

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) today announced that study results on investigational agents Opdivo (nivolumab), a PD-1 immune checkpoint inhibitor, elotuzumab, an antibody targeted against Signaling Lymphocyte Activation Molecule (SLAMF7), ulocuplumab, an anti-CXCR4 antibody, and Sprycel (dasatinib), will be featured in oral presentations at the 56th annual meeting of the American Society for Hematology (ASH) in San Francisco from December 6-9, 2014. Data will be presented in multiple hematologic malignancies, including Hodgkin lymphoma (HL), non-Hodgkin lymphoma, multiple myeloma, chronic-phase chronic myeloid leukemia (CP-CML), acute myeloid leukemia (AML) and T-Cell acute lymphoblastic leukemia. In May 2014, the U.S. Food and Drug Administration (FDA) granted Opdivo its first Breakthrough Therapy Designation for the treatment of patients with HL after failure of autologous stem cell transplant and brontuximab.

“The breadth of data we are presenting at ASH this year, including data on ulocuplumab and findings from our immuno-oncology development programs for Opdivo and elotuzumab, underscores our commitment to research and development in hematology and to improving outcomes for patients across a range of blood cancers,” said Michael Giordano, senior vice president, Head of Development, Oncology, Bristol-Myers Squibb.

**Opdivo (nivolumab) Oral Presentations in HL and Lymphoid Malignancies**

Data on Opdivo, an investigational PD-1 immune checkpoint inhibitor, will be presented during two oral presentations on Monday, December 8. At 7:00 a.m. PST, preliminary efficacy, safety and biomarker results will be presented from the relapsed or refractory HL cohort of CheckMate - 039, a Phase 1 dose escalation study of patients with relapsed or refractory hematologic malignancies (Abstract #289). At 7:30 a.m. PST, additional results from CheckMate-039 will be presented, including patients with relapsed or refractory non-Hodgkin lymphoma (Abstract #291).

**Elotuzumab Oral Presentation in Multiple Myeloma**

Final results from the Phase 1b/2 study of elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed or refractory multiple myeloma will be presented in an oral session on Monday, December 8 at 7:15 a.m. PST (Abstract #302).

In May 2014, the FDA granted elotuzumab Breakthrough Therapy Designation for use in combination with one of the commonly used chemotherapy treatments for multiple myeloma (lenalidomide, used in combination with dexamethasone) in patients who have received one or more prior treatments.

**Sprycel (dasatinib) Oral Presentations in CP-CML**

Results from two Sprycel studies will be highlighted in oral presentations, including five-year data from the Phase 3 trial, DASISION, comparing Sprycel to Gleevec® *(imatinib mesylate) in newly diagnosed CP-CML patients on Sunday, December 7 at 4:45 p.m. PST (Abstract #152) and seven-year data from a Phase 3 study of patients with Gleevec-resistant or intolerant CP-CML on Monday, December 8 at 3:30 p.m. PST (Abstract #520).
* Gleevec is a registered trademark of Novartis AG

**Additional Data Presentations**

Results from a Phase 1 study in relapsed/refractory AML, including safety, tolerability and clinical activity of the investigational anti-CXCR4 antibody ulocuplumab will be presented for the first time during an oral presentation on Monday, December 8 at 10:45 a.m. PST (Abstract #386). Additionally, results from a Phase 1 study of the safety and activity of BMS-906024, a notch inhibitor, in patients with relapsed T-Cell acute lymphoblastic leukemia, will be presented during a poster session on Saturday, December 6 between 5:30 and 7:30 p.m. PST (Abstract # 968).

Full session details of the 2014 Annual Meeting can be accessed on the ASH website: [http://www.bloodjournal.org/ash-annual-meeting-abstracts?sso-checked=true](http://www.bloodjournal.org/ash-annual-meeting-abstracts?sso-checked=true)

**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 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 its first 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 Biologics License Application (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 was also granted accelerated assessment by the EMA’s Committee for Medicinal Products for Human Use (CHMP). The EMA also validated for review the MAA for nivolumab in NSCLC.

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 Elotuzumab**

Elotuzumab is an investigational antibody targeted against Signaling Lymphocyte Activation Molecule (SLAMF7), a protein found on the surface of myeloma cells and Natural Killer (NK) cells, plasma cells and other immune cells, but not detectable in normal tissue. Based on current research, elotuzumab appears to have different effects when it binds to SLAMF7 on different cell types. The company is investigating whether through both direct activation and engagement of NK cells, elotuzumab may selectively target and kill SLAMF7 expressing myeloma cells.

Elotuzumab is being studied in combination with lenalidomide and low-dose dexamethasone in untreated multiple myeloma (ELOQUENT 1 study) as well as in multiple myeloma that has relapsed or no longer responds to treatment (ELOQUENT 2 study). It is also being studied as a single agent in smoldering multiple myeloma, which is a slow growing, early form of myeloma, as well as additional studies looking at elotuzumab in combination with different chemotherapies that are commonly used to treat myeloma at different stages of the disease.

In May 2014, the U.S. FDA granted elotuzumab Breakthrough Therapy Designation for use in combination with one of the commonly used chemotherapy treatments for multiple myeloma (lenalidomide, used in combination with dexamethasone) in patients who have received one or more prior treatments. Elotuzumab is being co-developed with AbbVie, with Bristol-Myers Squibb leading the commercialization of the agent.

**About Sprycel**

Sprycel was first approved by the FDA under accelerated review for the treatment of adults with CP Ph+ CML who are resistant or intolerant to prior therapy including imatinib in 2006. At that time, Sprycel was also approved for adults with Ph+ acute lymphoblastic leukemia (ALL) who are resistant or intolerant to prior therapy. Full approval was granted in May 2009. It is the first and only kinase inhibitor with survival data in its label for CP Ph+ CML patients who are resistant or intolerant to imatinib. Sprycel is now approved and marketed worldwide for these indications in more than 60 countries including the European Union (EU), Japan and Canada.

Sprycel is also an FDA-approved treatment for adults with newly diagnosed CP Ph+ CML (since October 2010). Sprycel received accelerated FDA approval for this indication. The effectiveness of Sprycel is based on cytogenetic response and major molecular response rates. The trial is ongoing and further data will be required to determine long-term outcome. Additional country approvals for this indication total more than 50.

**SPRYCEL® (dasatinib) INDICATIONS & IMPORTANT SAFETY INFORMATION**

**INDICATIONS**

SPRYCEL® (dasatinib) is indicated for the treatment of adults with:
Newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase. The effectiveness of SPRYCEL is based on cytogenetic and major molecular response rates. The trial is ongoing and further data will be required to determine long-term outcome.

Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib

**IMPORTANT SAFETY INFORMATION**

**Myelosuppression:**
Treatment with SPRYCEL® (dasatinib) can cause severe (NCI CTC Grade 3/4) thrombocytopenia, neutropenia, and anemia. Their occurrence is more frequent in patients with advanced phase CML or Ph+ ALL than in chronic phase CML. Myelosuppression was reported in patients with normal baseline laboratory values as well as in patients with pre-existing laboratory abnormalities.

- Perform complete blood counts (CBCs) weekly for the first 2 months and then monthly thereafter, or as clinically indicated
- Myelosuppression was generally reversible and usually managed by dose interruption, dose reduction, or discontinuation
- Hematopoietic growth factor has been used in patients with resistant myelosuppression

**Bleeding Related Events:**
SPRYCEL caused platelet dysfunction *in vitro* and thrombocytopenia in humans. In all clinical trials, severe central nervous system (CNS) hemorrhage, including fatalities, occurred in 1% of patients receiving SPRYCEL. Severe gastrointestinal hemorrhage, including fatalities, occurred in 4% of patients and generally required treatment interruptions and transfusions. Other cases of severe hemorrhage occurred in 2% of patients.

- Most bleeding events were associated with severe thrombocytopenia. Exercise caution in patients required to take medications that inhibit platelet function or anticoagulants

**Fluid Retention:**
SPRYCEL is associated with fluid retention. In clinical trials, fluid retention was severe in up to 10% of patients. Severe ascites, pulmonary edema, and generalized edema were each reported in ≤1% of patients.

- Patients who develop symptoms suggestive of pleural effusion, such as dyspnea or dry cough, should be evaluated by chest X-ray
- Severe pleural effusion may require thoracentesis and oxygen therapy
- Fluid retention was typically managed by supportive care measures that included diuretics or short courses of steroids

**QT Prolongation:**
*In vitro* data suggest that SPRYCEL has the potential to prolong cardiac ventricular repolarization (QT interval).

- In 865 patients with leukemia treated with SPRYCEL in five phase 2 single-arm studies, the maximum mean changes in QTcF (90% upper bound CI) from baseline ranged from 7.0 ms to 13.4 ms
- In clinical trials of patients treated with SPRYCEL (N=2440), 16 patients (1%) had QTc prolongation as an adverse reaction. Twenty-two patients (1%) experienced a QTcF >500 ms
- Administer SPRYCEL with caution to patients who have or may develop prolongation of QTc, including patients with hypokalemia, hypomagnesemia, or congenital long QT syndrome and patients taking anti-arrhythmic drugs, other medicinal products that lead to QT prolongation, and cumulative high-dose anthracycline therapy

- Correct hypokalemia or hypomagnesemia prior to SPRYCEL administration

**Congestive Heart Failure, Left Ventricular Dysfunction, and Myocardial Infarction:**
Cardiac adverse reactions were reported in 7% of 258 patients taking SPRYCEL, including 1.6% of patients with cardiomyopathy, heart failure congestive, diastolic dysfunction, fatal myocardial infarction, and left ventricular dysfunction.

- Monitor patients for signs or symptoms consistent with cardiac dysfunction and treat appropriately

**Pulmonary Arterial Hypertension (PAH):**
SPRYCEL may increase the risk of developing PAH, which may occur any time after initiation, including after more than one year of treatment. Manifestations include dyspnea, fatigue, hypoxia, and fluid retention. PAH may be reversible on discontinuation of SPRYCEL.

- Evaluate patients for signs and symptoms of underlying cardiopulmonary disease prior to initiating SPRYCEL and during treatment. If PAH is confirmed, SPRYCEL should be permanently discontinued

**Embryo-fetal Toxicity:**
SPRYCEL can cause fetal harm when administered to a pregnant woman. Adverse fetal and infant outcomes have been reported from women who have taken SPRYCEL during pregnancy. Transplacental transfer of dasatinib has been measured in fetal plasma and amniotic fluid and has been found to be comparable to those in maternal plasma.
If SPRYCEL is used during pregnancy, or if the patient becomes pregnant while taking SPRYCEL, the patient should be apprised of the potential hazard to the fetus.

Advise females of reproductive potential to avoid pregnancy during treatment with SPRYCEL.

**Nursing Mothers:**

It is unknown whether SPRYCEL is present in human milk; however, dasatinib was present in the milk of lactating rats.

Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue SPRYCEL.

**Drug Interactions:**

SPRYCEL is a CYP3A4 substrate and a weak time-dependent inhibitor of CYP3A4.

- Drugs that may increase SPRYCEL plasma concentrations are:
  - **CYP3A4 inhibitors:** Concomitant use of SPRYCEL and drugs that inhibit CYP3A4 should be avoided. If administration of a potent CYP3A4 inhibitor cannot be avoided, close monitoring for toxicity and a SPRYCEL dose reduction should be considered.
  - **Strong CYP3A4 inhibitors** (eg, ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole). If SPRYCEL must be administered with a strong CYP3A4 inhibitor, a dose decrease or temporary discontinuation should be considered.
    - Grapefruit juice may also increase plasma concentrations of SPRYCEL and should be avoided.

- Drugs that may decrease SPRYCEL plasma concentrations are:
  - **CYP3A4 inducers:** If SPRYCEL must be administered with a CYP3A4 inducer, a dose increase in SPRYCEL should be considered.
  - **Strong CYP3A4 inducers** (eg, dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, phenobarbital) should be avoided. Alternative agents with less enzyme induction potential should be considered. If the dose of SPRYCEL is increased, the patient should be monitored carefully for toxicity.
  - **St John’s Wort** may decrease SPRYCEL plasma concentrations unpredictably and should be avoided.
  - **Antacids** may decrease SPRYCEL drug levels. Simultaneous administration of SPRYCEL and antacids should be avoided. If antacid therapy is needed, the antacid dose should be administered at least 2 hours prior to or 2 hours after the dose of SPRYCEL.
  - **H2 antagonists/proton pump inhibitors** (eg, famotidine and omeprazole): Long-term suppression of gastric acid secretion by use of H2 antagonists or proton pump inhibitors is likely to reduce SPRYCEL exposure. Therefore, concomitant use of H2 antagonists or proton pump inhibitors with SPRYCEL is not recommended.

- Drugs that may have their plasma concentration altered by SPRYCEL are:
  - **CYP3A4 substrates** (eg, simvastatin) with a narrow therapeutic index should be administered with caution in patients receiving SPRYCEL.

**Adverse Reactions:**

The safety data reflect exposure to SPRYCEL in 258 patients with newly diagnosed chronic phase CML in a clinical trial (minimum of 36 months follow up; median duration of therapy was 37 months), and in 2182 patients with imatinib-resistant or -intolerant CML or Ph+ ALL in clinical trials (1520 patients had a minimum of 2 years follow up and 662 patients with chronic phase CML had a minimum of 60 months follow up).

The majority of SPRYCEL-treated patients experienced adverse reactions at some time. Patients aged 65 years and older are more likely to experience toxicity. In the newly diagnosed chronic phase CML trial, the cumulative discontinuation rate was 9% with a minimum of 36 months follow up. In patients resistant or intolerant to prior imatinib therapy, the discontinuation rate for SPRYCEL at 2 years for adverse reactions was: 15% of patients in chronic phase CML (all doses), 16% of patients in accelerated phase CML, 15% of patients in myeloid blast phase CML, 8% in lymphoid blast phase CML, and 8% in Ph+ ALL. In patients resistant or intolerant to prior imatinib therapy with chronic phase CML (minimum 60 months follow up), the rate of discontinuation for adverse reactions was 18% in patients treated with 100 mg once daily.

- In newly diagnosed chronic phase CML patients:
  - The most frequently reported serious adverse reactions included pleural effusion (4%), hemorrhage (2%), congestive heart failure (1%), pulmonary hypertension (1%), and pyrexia (1%).
  - The most frequently reported adverse reactions (reported in ≥10% of patients) included myelosuppression, fluid retention events (pleural effusion and superficial localized edema), diarrhea, headache, musculoskeletal pain, rash, and nausea.
  - Grade 3/4 laboratory abnormalities included neutropenia (24%), thrombocytopenia (19%), anemia (12%), hypophosphatemia (7%), hypocalcemia (3%), elevated bilirubin (1%), and elevated creatinine (1%).

- In patients resistant or intolerant to prior imatinib therapy:
  - The most frequently reported serious adverse reactions included pleural effusion (11%), gastrointestinal bleeding.
(4%), febrile neutropenia (4%), dyspnea (3%), pneumonia (3%), pyrexia (3%), diarrhea (3%), infection (2%), congestive heart failure/cardiac dysfunction (2%), pericardial effusion (1%), and CNS hemorrhage (1%)

- The most frequently reported adverse reactions (reported in ≥20% of patients) included myelosuppression, fluid retention events, diarrhea, headache, dyspnea, skin rash, fatigue, nausea, and hemorrhage
- Grade 3/4 hematologic laboratory abnormalities in chronic phase CML patients resistant or intolerant to prior imatinib therapy who received SPRYCEL 100 mg once daily with a minimum follow up of 60 months included neutropenia (36%), thrombocytopenia (24%) and anemia (13%). Other grade 3/4 laboratory abnormalities included: hypophosphatemia (10%) and hypokalemia (2%)
  - Among chronic phase CML patients with resistance or intolerance to prior imatinib therapy, cumulative Grade 3 or 4 cytopenias were similar at 2 and 5 years including: neutropenia (36% vs 36%), thrombocytopenia (23% vs 24%), and anemia (13% vs 13%)
  - Grade 3/4 elevations of transaminase or bilirubin and Grade 3/4 hypocalcemia, hypokalemia, and hypophosphatemia were reported in patients with all phases of CML
    - Elevations in transaminase or bilirubin were usually managed with dose reduction or interruption
    - Patients developing Grade 3/4 hypocalcemia during the course of SPRYCEL therapy often had recovery with oral calcium supplementation

Please see the full Prescribing Information at www.bms.com.

SPRYCEL is a registered trademark of Bristol-Myers Squibb Company.

**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 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, or any other compounds mentioned in this release, 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.

**Language:**

English

**Contact:**

Bristol-Myers Squibb Company
Media:
Sarah Koenig, 609-252-4145
sarah.koenig@bms.com

or

Chrissy Trank, 609-252-3418
Christina.trank@bms.com

or

Investors:
Ranya Dajani, 609-252-5330
ranya.dajani@bms.com

or