Seattle Genetics and Bristol-Myers Squibb Highlight
First Data from Phase 1/2 Study Evaluating
ADCETRIS® (Brentuximab Vedotin) in Combination
with Opdivo (nivolumab) in Relapsed or Refractory
Hodgkin Lymphoma at ASH Annual Meeting

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- Combination Data Showed 90 Percent Objective Response Rate and
62 Percent Complete Response Rate with an Acceptable Safety Profile
in Pre-Transplant Relapsed or Refractory Classical Hodgkin Lymphoma
Patients -

- Data Support Continued Clinical Investigation of ADCETRIS and
Opdivo Combination in Hodgkin Lymphoma -

SAN DIEGO--(BUSINESS WIRE)--Seattle Genetics, Inc. (NASDAQ:SGEN) and Bristol-Myers Squibb Company (NYSE:BMY) today highlighted the first reported data from an ongoing phase 1/2 clinical trial evaluating ADCETRIS (brentuximab vedotin) in combination with Opdivo (nivolumab) in relapsed or refractory classical Hodgkin lymphoma (HL) at the 58th American Society of Hematology (ASH) Annual Meeting and Exposition taking place in San Diego, California, December 3-6, 2016. The data reported from 42 patients, including 29 evaluable for response, were featured in an oral presentation and selected to be included in the 2017 Highlights of ASH post-meeting program. ADCETRIS is an antibody-drug conjugate (ADC) directed to CD30, a defining marker of classical HL that plays a role in tumor growth and survival. Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to harness the body’s own immune system to help restore anti-tumor immune response. ADCETRIS and Opdivo are not approved in combination for the treatment of relapsed or refractory HL or for other indications.

“The phase 1/2 study combining the antibody-drug conjugate ADCETRIS with the PD-1 immune checkpoint inhibitor Opdivo is a promising investigational approach as it combines a targeted therapy with a therapy designed to activate the immune system and the combination may have synergistic activity,” said Alex Herrera, M.D., lead trial investigator and assistant professor at the City of Hope Medical Center, Duarte, California. “The preliminary results are compelling and support further exploration of this novel regimen, free of traditional chemotherapy.”

“We are evaluating ADCETRIS broadly as the foundation of care for CD30-expressing lymphomas, including combination strategies that have the potential to improve efficacy,” said Jonathan Drachman, M.D., Chief Medical Officer and Executive Vice President, Research and Development at Seattle Genetics. “Preliminary data from the trial evaluating ADCETRIS in combination with Opdivo as pre-transplant salvage therapy for classical HL patients demonstrate a 90 percent objective response rate, with a 62 percent complete response rate and an acceptable safety profile. We look forward to further evaluation of this innovative combination regimen in other disease settings, including frontline older HL patients and CD30-expressing non-Hodgkin lymphoma, in partnership with Bristol-Myers Squibb.”

Fouad Namouni, M.D., Head of Development, Oncology, Bristol-Myers Squibb, commented, “With these new data presented at ASH, Bristol-Myers Squibb continues its efforts to strengthen its broad Immuno-Oncology and hematology development programs for Opdivo. Through our continued partnership with Seattle Genetics, we hope to build on the significant progress we’ve made with Opdivo as monotherapy and deliver new combination treatment options with the potential to improve the lives of patients impacted by blood cancers with high unmet needs.”

Preliminary Results from a Phase 1/2 Study of Brentuximab Vedotin in Combination with Nivolumab in Patients with Relapsed or Refractory Hodgkin Lymphoma (Abstract #1105, oral presentation at 4:30 p.m. PT)

Data were reported from 42 patients with relapsed or refractory HL after failure of frontline therapy who received the combination regimen of ADCETRIS plus Opdivo. Patients were treated once every three weeks with up to four cycles of combination therapy. After completion of the fourth cycle of treatment, patients were eligible to undergo an autologous


stem cell transplant (ASCT). The median age of patients was 37 years. The majority of patients (88 percent) were refractory or had progressed after receiving the standard of care frontline treatment ABVD (Adriamycin, bleomycin, vinblastine and dacarbazine).

Key findings presented include:

- Of 29 response-evaluable patients, 26 patients (90 percent) had an objective response, including 18 patients (62 percent) with a complete metabolic response and eight patients (28 percent) with a partial metabolic response. One patient (three percent) had stable disease and two patients (seven percent) had progressive disease.

- Of the 42 patients enrolled, all patients (100 percent) received one or more dose of the study therapies, 12 patients (29 percent) remain on treatment, 28 patients (67 percent) have completed treatment and two patients (five percent) discontinued prior to the end of treatment. At the time of data analysis in the ongoing trial, nine patients (21 percent) initiated an ASCT and two patients (five percent) received an alternative salvage therapy prior to ASCT. Preliminary analysis shows no impact of ADCETRIS and Opdivo combination on stem cell mobilization or engraftment.

- The median number of doses administered for both ADCETRIS and Opdivo was four. Of the 42 patients, no patients had a dose reduction during treatment due to an adverse event for either therapy. Dose delays occurred for three patients (seven percent) with ADCETRIS treatment and four patients (10 percent) with Opdivo treatment. Reasons for dose delays were urticaria, thrombosis, elevated lipase, chills and hypoxia.

- The most common adverse events of any grade occurring prior to ASCT in more than 20 percent of patients were fatigue, nausea, infusion related reaction, pruritus and rash. One patient had a treatment-related serious adverse event after Cycle 1 of ADCETRIS, with Grade 3 dehydration, Grade 1 asthenia and nausea, Grade 2 hypercalcemia and malaise.

- Infusion-related reactions (IRR) were observed in 38 percent of patients and most symptoms included flushing and nausea (14 percent each); chest discomfort, dyspnea, urticaria (12 percent each); cough and pruritis (10 percent each). A protocol amendment was made requiring premedication with low-dose corticosteroids and antihistamine. No patients discontinued treatment due to an IRR.

- Potential immune-related adverse events included IRR (36 percent [one IRR not reported as associated with infusion]; Grade 1 or 2), rash (29 percent; Grade 1 or 2), diarrhea (26 percent; Grade 1 or 2), transaminase elevation (10 percent; Grade 1 and 3/4) and hypothyroidism (five percent; Grade 2). There were no occurrences of pneumonitis or colitis.

ADCETRIS and Opdivo are being evaluated as combination therapy in multiple ongoing phase 1/2 clinical trials. In addition to the study presented at ASH, a trial titled “A Safety and Effectiveness Study of Nivolumab in Combination With Brentuximab Vedotin to Treat Non-Hodgkin Lymphomas” is ongoing and focused on patients with relapsed or refractory disease, including diffuse large B-cell lymphoma (DLBCL), and other rare subtypes of B-cell, including mediastinal B-cell lymphoma and mediastinal gray zone lymphoma. In addition, the companies recently extended the clinical evaluation of ADCETRIS and Opdivo into a clinical trial evaluating the combination as frontline treatment for older HL patients.

About Classical Hodgkin Lymphoma

Lymphoma is a general term for a group of cancers that originate in the lymphatic system and is the most common type of blood cancer. There are two major categories of lymphoma: HL, also known as Hodgkin disease, and non-Hodgkin lymphoma. HL is a cancer that starts in white blood cells called lymphocytes, which are part of the body’s immune system. The disease is most often diagnosed in early adulthood (ages 20-40) and late adulthood (older than 55 years of age). Classical Hodgkin lymphoma is the most common type of HL, accounting for 95% of cases. Classical HL is distinguished from other lymphomas by the characteristic presence of CD30-positive Reed-Sternberg cells.

According to the American Cancer Society, approximately 8,500 cases of HL will be diagnosed in the United States during 2016 and more than 1,100 will die from the disease. According to the Lymphoma Coalition, over 62,000 people worldwide are diagnosed with HL each year and approximately 25,000 people die each year from this cancer. In the European Union, about 12,200 new cases and 2,600 deaths occurred in 2012 as a result of HL.

About ADCETRIS (Brentuximab Vedotin)

ADCETRIS is being evaluated broadly in more than 70 ongoing clinical trials, including three phase 3 studies, the ongoing ECHELON-1 trial in frontline classical Hodgkin lymphoma and the ongoing ECHELON-2 trial in frontline mature T-cell lymphomas, as well as the completed ALCANZA trial in cutaneous T-cell lymphoma for which a supplemental BLA is planned in the first half of 2017.

ADCETRIS is an ADC comprising an anti-CD30 monoclonal antibody attached to a protease-cleavable linker to a microtubule disrupting agent, monomethyl auristatin E (MMAE), utilizing Seattle Genetics’ proprietary technology. The ADC employs a linker system that is designed to be stable in the bloodstream but to release MMAE upon internalization into CD30-expressing tumor cells.

ADCETRIS for intravenous injection has received approval from the FDA for three indications: (1) regular approval for the treatment of patients with classical Hodgkin lymphoma after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates, (2) regular approval for the treatment of classical Hodgkin lymphoma patients at high risk of relapse or progression as post-auto-HSCT consolidation, and (3) accelerated approval for the treatment of patients with systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen. The sALCL indication is approved under accelerated approval based on overall response rate. Continued approval for the sALCL indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Health Canada granted ADCETRIS approval with conditions for relapsed or refractory Hodgkin lymphoma and sALCL.

ADCETRIS was granted conditional marketing authorization by the European Commission in October 2012 for two indications: (1) for the treatment of adult patients with relapsed or refractory CD30-positive Hodgkin lymphoma following autologous stem cell transplantation (ASCT). The median age of patients was 37 years. The majority of patients (88 percent) were refractory or had progressed after receiving the standard of care frontline treatment ABVD (Adriamycin, bleomycin, vinblastine and dacarbazine).
ADCETRIS has received marketing authorization by regulatory authorities in 65 countries. See important safety information below.

Seattle Genetics and Takeda are jointly developing ADCETRIS. Under the terms of the collaboration agreement, Seattle Genetics has U.S. and Canadian commercialization rights and Takeda has rights to commercialize ADCETRIS in the rest of the world. Seattle Genetics and Takeda are funding joint development costs for ADCETRIS on a 50:50 basis, except in Japan where Takeda is solely responsible for development costs.

About Opdivo

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body’s own immune system to help restore anti-tumor immune response. By harnessing the body’s own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers.

Opdivo’s leading global development program is based on Bristol-Myers Squibb’s scientific expertise in the field of Immuno-Oncology and includes a broad range of clinical trials across all phases, including Phase 3, in a variety of tumor types. To date, the Opdivo clinical development program has enrolled more than 25,000 patients. The Opdivo trials have contributed to gaining a deeper understanding of the potential role of biomarkers in patient care, particularly regarding how patients may benefit from Opdivo across the continuum of PD-L1 expression.

In July 2014, Opdivo was the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world. Opdivo is currently approved in more than 57 countries, including the United States, the European Union and Japan. In October 2015, the company’s Opdivo + Yervoy combination was the first Immuno-Oncology combination to receive regulatory approval for the treatment of metastatic melanoma and is currently approved in more than 47 countries, including the United States and the European Union.

About Seattle Genetics

Seattle Genetics is an innovative biotechnology company that develops and commercializes novel antibody-based therapies for the treatment of cancer. The company’s industry-leading antibody-drug conjugate (ADC) technology harnesses the targeting ability of antibodies to deliver cell-killing agents directly to cancer cells. ADCETRIS® (brentuximab vedotin), the company’s lead product, in collaboration with Takeda Pharmaceutical Company Limited, is the first in a new class of ADCs commercially available globally in 65 countries for relapsed classical Hodgkin lymphoma and relapsed systemic anaplastic large cell lymphoma (sALCL). Seattle Genetics is also advancing vadastuximab talirine (SGN-CD33A; 33A), an ADC in a phase 3 trial for acute myeloid leukemia. Headquartered in Bothell, Washington, Seattle Genetics has a robust pipeline of innovative therapies for blood-related cancers and solid tumors designed to address significant unmet medical needs and improve treatment outcomes for patients. The company has collaborations for its proprietary ADC technology with a number of companies including AbbVie, Astellas, Bayer, Genentech, GlaxoSmithKline and Pfizer. More information can be found at www.seattlegenetics.com

Bristol-Myers Squibb: At the Forefront of Immuno-Oncology Science & Innovation

At Bristol-Myers Squibb, patients are at the center of everything we do. Our vision for the future of cancer care is focused on researching and developing transformational Immuno-Oncology (I-O) medicines that will raise survival expectations in hard-to-treat cancers and will change the way patients live with cancer.

We are leading the scientific understanding of I-O through our extensive portfolio of investigational and approved agents, including the first combination of two I-O agents in metastatic melanoma, and our differentiated clinical development program, which is studying broad patient populations across more than 20 types of cancers with 11 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs uniquely position us to advance the science of combinations across multiple tumors and potentially deliver the next wave of I-O combination regimens with a sense of urgency. We also continue to pioneer research that will help facilitate a deeper understanding of the role of immune biomarkers and inform which patients will benefit most from I-O therapies.

We understand making the promise of I-O a reality for the many patients who may benefit from these therapies requires not only innovation on our part but also close collaboration with leading experts in the field. Our partnerships with academia, government, advocacy and biotech companies support our collective goal of providing new treatment options to advance the standards of clinical practice.

ADCETRIS (brentuximab vedotin) U.S. Important Safety Information

BOXED WARNING
Progressive multifocal leukoencephalopathy (PML): JC virus infection resulting in PML and death can occur in patients receiving ADCETRIS.

Contraindication
ADCETRIS is contraindicated with concomitant bleomycin due to pulmonary toxicity (e.g., interstitial infiltration and/or inflammation).

Warnings and Precautions
- Peripheral neuropathy (PN): ADCETRIS treatment causes a PN that is predominantly sensory. Cases of motor PN have also been reported. ADCETRIS-induced PN is cumulative. Monitor patients for symptoms of neuropathy, such as
hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain or weakness and institute dose modifications accordingly.

- Anaphylaxis and infusion reactions: Infusion-related reactions, including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If an infusion-related reaction occurs, interrupt the infusion and institute appropriate medical management. If anaphylaxis occurs, immediately and permanently discontinue the infusion and administer appropriate medical therapy. Patients who experienced a prior infusion-related reaction should be premedicated for subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid.

- Hematologic toxicities: Prolonged (≥1 week) severe neutropenia and Grade 3 or 4 thrombocytopenia or anemia can occur with ADCETRIS. Febrile neutropenia has been reported with ADCETRIS. Monitor complete blood counts prior to each dose of ADCETRIS and consider more frequent monitoring for patients with Grade 3 or 4 neutropenia. Monitor patients for fever. If Grade 3 or 4 neutropenia develops, consider dose delays, reductions, discontinuation, or G-CSF prophylaxis with subsequent doses.

- Serious infections and opportunistic infections: Infections such as pneumonia, bacteremia, and sepsis or septic shock (including fatal outcomes) have been reported in patients treated with ADCETRIS. If SJS or TEN occurs, discontinue ADCETRIS and institute appropriate medical therapy. Patients who experienced a prior infusion-related reaction should be premedicated for subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid.

- Tumor lysis syndrome: Closely monitor patients with rapidly proliferating tumor and high tumor burden.

- Increased toxicity in the presence of severe renal impairment: The frequency of ≥Grade 3 adverse reactions and deaths was greater in patients with severe renal impairment compared to patients with normal renal function. Avoid the use of ADCETRIS in patients with severe renal impairment.

- Increased toxicity in the presence of moderate or severe hepatic impairment: The frequency of ≥Grade 3 adverse reactions and deaths was greater in patients with moderate or severe hepatic impairment compared to patients with normal hepatic function. Avoid the use of ADCETRIS in patients with moderate or severe hepatic impairment.

- Hepatotoxicity: Serious cases of hepatotoxicity, including fatal outcomes, have occurred with ADCETRIS. Cases were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, and occurred after the first dose of ADCETRIS or rechallenge. Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may also increase the risk. Monitor liver enzymes and bilirubin. Patients experiencing new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation of ADCETRIS.

- Progressive multifocal leukoencephalopathy (PML): JC virus infection resulting in PML and death has been reported in ADCETRIS-treated patients. First onset of symptoms occurred at various times from initiation of ADCETRIS therapy, with some cases occurring within 3 months of initial exposure. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression. Consider the diagnosis of PML in any patient presenting with new-onset signs and symptoms of central nervous system abnormalities. Hold ADCETRIS if PML is suspected and discontinue ADCETRIS if PML is confirmed.

- Pulmonary toxicity: Events of noninfectious pulmonary toxicity including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, some with fatal outcomes, have been reported. Monitor patients for signs and symptoms of pulmonary toxicity, including cough and dyspnea. In the event of new or worsening pulmonary symptoms, hold ADCETRIS during evaluation and until symptomatic improvement.

- Serious dermatologic reactions: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), including fatal outcomes, have been reported with ADCETRIS. If SJS or TEN occurs, discontinue ADCETRIS and administer appropriate medical therapy.

- Gastrointestinal (GI) complications: Fatal and serious GI complications, including perforation, hemorrhage, erosion, ulcer, intestinal obstruction, enterocolitis, neutropenic colitis, and ileus have been reported in ADCETRIS-treated patients. Lymphoma with preexisting GI involvement may increase the risk of perforation. In the event of new or worsening GI symptoms, perform a prompt diagnostic evaluation and treat appropriately.

- Embryo-fetal toxicity: Based on the mechanism of action and findings in animals, ADCETRIS can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

Adverse Reactions

In two uncontrolled single-arm trials of ADCETRIS as monotherapy in 160 patients with relapsed classical HL and sALCL, the most common adverse reactions (≥20%), regardless of causality, were: neutropenia, peripheral sensory neuropathy, fatigue, nausea, anemia, upper respiratory tract infection, diarrhea, pyrexia, rash, thrombocytopenia, cough and vomiting.

In a placebo-controlled trial of ADCETRIS in 329 patients with classical HL at high risk of relapse or progression post-auto-HSCT, the most common adverse reactions (≥20%) in the ADCETRIS-treatment arm (167 patients), regardless of causality, were: neutropenia, peripheral sensory neuropathy, thrombocytopenia, anemia, upper respiratory tract infection, fatigue, peripheral motor neuropathy, nausea, cough, and diarrhea.

Drug Interactions

Concomitant use of strong CYP3A4 inhibitors or inducers, or P-gp inhibitors, has the potential to affect the exposure to monomethyl auristatin E (MMAE).

Use in Specific Populations

MMAE exposure and adverse reactions are increased in patients with moderate or severe hepatic impairment or severe renal impairment. Avoid use.

Advising females of reproductive potential to avoid pregnancy during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.
Advertise males with female sexual partners of reproductive potential to use effective contraception during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

Advise patients to report pregnancy immediately and avoid breastfeeding while receiving ADCETRIS.

For additional Important Safety Information, including Boxed WARNING, please see the full Prescribing Information for ADCETRIS at www.seattlegenetics.com or www.ADCETRIS.com.

U.S. FDA-APPROVED INDICATIONS FOR OPDIVO ®

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the treatment of patients with unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO® (nivolumab) is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.

OPDIVO® (nivolumab) is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

OPDIVO® (nivolumab) is indicated for the treatment of patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

OPDIVO® (nivolumab) is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

IMPORTANT SAFETY INFORMATION

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions. 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), adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and before each dose.

Permanently discontinue YERVOY and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.

Immune-Mediated Pneumonitis

OPDIVO can cause immune-mediated pneumonitis. Fatal cases have been reported. Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis. Administer corticosteroids for Grade 2 or more severe pneumonitis. Permanently discontinue for Grade 3 or 4 and withhold until resolution for Grade 2. In patients receiving OPDIVO monotherapy, fatal cases of immune-mediated pneumonitis have occurred. Immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated pneumonitis occurred in 6% (25/407) of patients.

In CheckMate 205 and 039, pneumonitis, including interstitial lung disease, occurred in 4.9% (13/263) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 3.4% (9/263) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=8).

Immune-Mediated Colitis

OPDIVO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO monotherapy for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon re-initiation of OPDIVO. When administered with YERVOY, withhold OPDIVO and YERVOY for Grade 2 and permanently discontinue for Grade 3 or 4 or recurrent colitis. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated colitis occurred in 26% (107/407) of patients including three fatal cases.

In a separate Phase 3 study of YERVOY 3 mg/kg, 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%) patients. Across all YERVOY-
treated patients in that study (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis.

Immune-Mediated Hepatitis
OPDIVO can cause immune-mediated hepatitis. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater transaminase elevations. Withhold for Grade 2 and permanently discontinue for Grade 3 or 4 immune-mediated hepatitis. In patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated hepatitis occurred in 13% (51/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, 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%.

Immune-Mediated Neuropathies
In a separate Phase 3 study of YERVOY 3 mg/kg, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported.

Immune-Mediated Endocrinopathies
OPDIVO can cause immune-mediated hypophysitis, immune-mediated adrenal insufficiency, autoimmune thyroid disorders, and Type 1 diabetes mellitus. Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency, thyroid function prior to and periodically during treatment, and hyperglycemia. Administer hormone replacement as clinically indicated and corticosteroids for Grade 2 or greater hypophysitis. Withhold for Grade 2 or 3 and permanently discontinue for Grade 4 hypophysitis. Administer corticosteroids for Grade 3 or 4 adrenal insufficiency. Withhold for Grade 2 and permanently discontinue for Grade 3 or 4 adrenal insufficiency. Administer hormone-replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 hyperglycemia.

In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients. In patients receiving OPDIVO with YERVOY, hypophysitis occurred in 9% (36/407) of patients. In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994) of patients. In patients receiving OPDIVO with YERVOY, adrenal insufficiency occurred in 5% (21/407) of patients. In patients receiving OPDIVO monotherapy, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 9% (171/1994) of patients. Hyperthyroidism occurred in 2.7% (54/1994) of patients receiving OPDIVO monotherapy. In patients co-administering OPDIVO with YERVOY, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving OPDIVO with YERVOY. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO with YERVOY, diabetes occurred in 1.5% (6/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, 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.

Immune-Mediated Nephritis and Renal Dysfunction
OPDIVO can cause immune-mediated nephritis. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grades 2-4 increased serum creatinine. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 increased serum creatinine. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients.

Immune-Mediated Skin Adverse Reactions and Dermatitis
OPDIVO can cause immune-mediated rash, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrosis (TEN), in some cases with fatal outcome. Administer corticosteroids for Grade 3 or 4 rash. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 rash. For symptoms or signs of SJS or TEN, withhold OPDIVO and refer the patient for specialized care for assessment and treatment; if confirmed, permanently discontinue. In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated rash occurred in 22.6% (92/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, severe, life-threatening, or fatal immune-mediated dermatitis (eg, Stevens-Johnson syndrome, toxic epidermal necrosis, 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 necrosis. 1 additional patient required hospitalization for severe dermatitis.

Immune-Mediated Encephalitis
OPDIVO can cause immune-mediated encephalitis. Evaluation of patients with neurologic symptoms may include, but not be limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Withhold OPDIVO in patients with new-onset moderate to severe neurologic signs or symptoms and evaluate to rule out other or thyroid-specific etiologies are ruled out, administer corticosteroids and permanently discontinue OPDIVO for immune-mediated encephalitis. In patients receiving OPDIVO monotherapy, encephalitis occurred in 0.2% (3/1994) of patients. Fatal limbic encephalitis occurred in one patient after 7.2 months of exposure despite discontinuation of OPDIVO and administration of corticosteroids. Encephalitis occurred in one patient receiving OPDIVO with YERVOY (0.2%) after 1.7 months of exposure.

Other Immune-Mediated Adverse Reactions
Based on the severity of adverse reaction, permanently discontinue or withhold treatment, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy. Across clinical trials of OPDIVO the following clinically significant immune-mediated adverse reactions occurred in <1.0% of patients receiving OPDIVO: uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), myositis, myocarditis, rhabdomyolysis, motor dysfunction, vasculitis, and myasthenic syndrome.

**Infusion Reactions**

OPDIVO can cause severe infusion reactions, which have been reported in <1.0% of patients in clinical trials. Discontinue OPDIVO in patients with Grade 3 or 4 infusion reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2. In patients receiving OPDIVO monotherapy, infusion-related reactions occurred in 6.4% (127/1994) of patients. In patients receiving OPDIVO with YERVOY, infusion-related reactions occurred in 2.5% (10/407) of patients.

**Complications of Allogeneic HSCT after OPDIVO**

Complications, including fatal events, occurred in patients who received allogeneic HSCT after OPDIVO. Outcomes were evaluated in 17 patients from CheckMate 205 and 039, who underwent allogeneic HSCT after discontinuing OPDIVO (15 with reduced-intensity conditioning, 2 with myeloablative conditioning). Thirty-five percent (6/17) of patients died from complications of allogeneic HSCT after OPDIVO. Five deaths occurred in the setting of severe or refractory GVHD. Grade 3 or higher acute GVHD was reported in 29% (5/17) of patients. Hyperacute GVHD was reported in 20% (n=2) of patients. A steroid-requiring febrile syndrome, without an identified infectious cause, was reported in 35% (n=6) of patients. Two cases of encephalitis were reported: Grade 3 (n=1) lymphocytic encephalitis without an identified infectious cause, and Grade 3 (n=1) suspected viral encephalitis. Hepatic veno-occlusive disease (VOD) occurred in one patient, who received reduced-intensity conditioned allogeneic HSCT and died of GVHD and multi-organ failure. Other cases of hepatic VOD after reduced-intensity conditioned allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor blocking antibody before transplantation. Cases of fatal hyperacute GVHD have also been reported. These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.

Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervene promptly.

**Embryo-Fetal Toxicity**

Based on their mechanisms of action, OPDIVO and YERVOY can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with an OPDIVO- or YERVOY- containing regimen and for at least 5 months after the last dose of OPDIVO.

**Lactation**

It is not known whether OPDIVO or YERVOY is present in human milk. Because many drugs, including antibodies, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from an OPDIVO-containing regimen, advise women to discontinue breastfeeding during treatment. Advise women to discontinue nursing during treatment with YERVOY and for 3 months following the final dose.

**Serious Adverse Reactions**

In CheckMate 037, serious adverse reactions occurred in 41% of patients receiving OPDIVO (n=268). Grade 3 and 4 adverse reactions occurred in 42% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse drug reactions reported in 2% to <5% of patients receiving OPDIVO were abdominal pain, hyponatremia, increased aspartate aminotransferase, and increased lipase. In CheckMate 066, serious adverse reactions occurred in 36% of patients receiving OPDIVO (n=206). Grade 3 and 4 adverse reactions occurred in 41% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of patients receiving OPDIVO were gamma-glutamyltransferase increase (3.9%) and diarrhea (3.4%). In CheckMate 067, serious adverse reactions occurred in 49% of patients receiving OPDIVO (n=418). The most frequent Grade 3 and 4 adverse reactions occurred in 46% of patients receiving OPDIVO (n=418). The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In CheckMate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). The most frequent serious adverse reactions reported in ≥2% of patients were acute kidney injury, pleural effusion, pneumonia, diarrhea, and hypercalcemia. In CheckMate 205 and 039, among all patients (safety population [n=263]), adverse reactions leading to permanent discontinuation (43% and 14%) or to dosing delays (55% and 28%), and Grade 3 or 4 adverse reactions (72% and 44%) all occurred more frequently in the OPDIVO plus YERVOY arm (n=313) relative to the OPDIVO arm (n=313). The most frequent (≥10%) serious adverse reactions in the OPDIVO plus YERVOY arm and the OPDIVO arm, respectively, were diarrhea (13% and 2.6%), colitis (10% and 1.6%), and pyrexia (10% and 0.6%). In CheckMate 017 and 057, serious adverse reactions occurred in 48% of patients receiving OPDIVO (n=418). The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In CheckMate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). The most frequent serious adverse reactions reported in ≥2% of patients were acute kidney injury, pleural effusion, pneumonia, diarrhea, and hypercalcemia. In CheckMate 205 and 039, among all patients (safety population [n=263]), adverse reactions leading to discontinuation (42%) or to dosing delays (23%) occurred. The most frequent serious adverse reactions reported in ≥1% of patients were infusion-related reaction, pneumonia, pleural effusion, pyrexia, rash and pneumonitis. Ten patients died from causes other than disease progression, including 6 who died from complications of allogeneic HSCT. Serious adverse reactions occurred in 21% of patients in the safety population (n=263) and 27% of patients in the subset of patients evaluated for efficacy (efficacy population [n=95]). In CheckMate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO. The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, dyspnea, respiratory failure, respiratory tract infections, and sepsis.

**Common Adverse Reactions**

In CheckMate 037, the most common adverse reactions (≥20%) reported with OPDIVO (n=268) was rash (21%). In CheckMate 066, the most common adverse reactions (≥20%) reported with OPDIVO (n=206) vs dacarbazine (n=205) were fatigue (49% vs 39%), musculoskeletal pain (32% vs 25%), rash (28% vs 12%), and pruritus (23% vs 12%). In CheckMate 067, the most
common (≥20%) adverse reactions in the ODPIVO plus YERVOY arm (n=313) were fatigue (59%), rash (53%), diarrhea (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common (≥20%) adverse reactions in the ODPIVO (n=313) arm were fatigue (53%), rash (40%), diarrhea (31%), and nausea (28%). In CheckMate 017 and 057, the most common adverse reactions (≥20%) in patients receiving ODPIVO (n=418) were fatigue, musculoskeletal pain, cough, dyspnea, and decreased appetite. In CheckMate 025, the most common adverse reactions (≥20%) reported in patients receiving ODPIVO (n=406) vs everolimus (n=397) were asthenic conditions (56% vs 57%), cough (34% vs 38%), nausea (28% vs 29%), rash (28% vs 36%), dyspnea (27% vs 31%), diarrhea (25% vs 32%), constipation (23% vs 18%), decreased appetite (23% vs 30%), back pain (21% vs 16%), and arthralgia (20% vs 14%). In CheckMate 205 and 039, among all patients (safety population [n=263]) and the subset of patients in the efficacy population (n=95), respectively, the most common adverse reactions (≥20%) were fatigue (32% and 43%), upper respiratory tract infection (28% and 48%), pyrexia (24% and 35%), diarrhea (23% and 30%), and cough (22% and 25%). In the subset of patients in the efficacy population (n=95), the most common adverse reactions also included rash (31%), musculoskeletal pain (27%), pruritus (25%), nausea (23%), arthralgia (21%), and peripheral neuropathy (21%). In CheckMate 141, the most common adverse reactions (≥10%) in patients receiving ODPIVO were cough and dyspnea at a higher incidence than investigator's choice.

In a separate Phase 3 study of YERVOY 3 mg/kg, 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%).

**CheckMate Trials and Patient Populations**

- **CheckMate 067** – advanced melanoma alone or in combination with YERVOY; **CheckMate 037 and 066** – advanced melanoma; **CheckMate 017** – squamous non-small cell lung cancer (NSCLC); **CheckMate 057** – non-squamous NSCLC; **CheckMate 025** – renal cell carcinoma; **CheckMate 205/039** – classical Hodgkin lymphoma; **CheckMate 141** – squamous cell carcinoma of the head and neck

Please see U.S. Full Prescribing Information for ODPIVO and YERVOY, including [Boxed WARNING regarding immune-mediated adverse reactions](#) for YERVOY.

**About the Bristol-Myers Squibb and Ono Pharmaceutical Collaboration**

In 2011, through a collaboration agreement with Ono Pharmaceutical Co., Ltd (Ono), 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 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 biopharmaceutical 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 us at [BMS.com](http://www.BMS.com) or follow us on [LinkedIn](http://www.LinkedIn.com), [Twitter](http://www.Twitter.com), [YouTube](http://www.YouTube.com) and [Facebook](http://www.Facebook.com).

**Seattle Genetics Forward-Looking Statement**

Certain of the statements made in this press release are forward looking, such as those, among others, relating to the therapeutic and commercial potential of ADCETRIS, including ADCETRIS’ potential as a combination treatment with Opdivo, the anticipated benefits of Seattle Genetics’ ADCETRIS clinical development program, and the potential submission of applications (e.g., a supplemental Biologics License Application in the U.S.) seeking label expansion for ADCETRIS. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include the risks of adverse events associated with ADCETRIS use, negative or unexpected results from the ADCETRIS and Opdivo combination trials, and adverse regulatory actions affecting ADCETRIS, all of which could result in Seattle Genetics being unable to expand ADCETRIS’ labeled indications. Seattle Genetics may also experience delays in the conduct of and obtaining data from the ADCETRIS and Opdivo combination studies and its other clinical trials, in each case for a variety of reasons, including the inherent difficulty and uncertainty of pharmaceutical product development. More information about the risks and uncertainties faced by Seattle Genetics is contained under the caption “Risk Factors” included in the company’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 filed with the Securities and Exchange Commission.

Seattle Genetics disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

**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. 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, 2015 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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#BMY to present new #cancer research on relapsed/refractory Hodgkin lymphoma at #ASH16: