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## Progression-Free Survival Data from ECHO-202 Trial of Incyte's Epacadostat in Combination with Merck's KEYTRUDA® (pembrolizumab) Underscore Durability of Response in Patients with Advanced Melanoma

September 9, 2017

*Updated Data to be Presented at ESMO 2017 Congress*

WILMINGTON, Del. & KENILWORTH, N.J.--(BUSINESS WIRE)--Sep. 9, 2017-- Incyte Corporation (Nasdaq:INCY) and Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced updated data from the ongoing Phase 1/2 ECHO-202 trial (KEYNOTE-037) evaluating epacadostat, Incyte's selective IDO1 enzyme inhibitor, in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, in patients with advanced melanoma. Among all patients with advanced melanoma, including treatment-naïve and treatment-experienced, data showed an overall response rate (ORR) of 56 percent (n=35/63) in patients treated with the combination of epacadostat and KEYTRUDA; median progression-free survival (PFS) was 12.4 months, with PFS rates of 65 percent at six months, 52 percent at 12 months, and 49 percent at 18 months. Results were generally consistent across dosing schedules of epacadostat combined with KEYTRUDA, including epacadostat 100 mg BID, the epacadostat dose being studied in the Phase 3 ECHO-301 trial.

This Smart News Release features multimedia. View the full release here: <http://www.businesswire.com/news/home/20170909005016/en/>



# MERCK

These results will be presented at the European Society for Medical Oncology (ESMO) 2017 Congress in Madrid, Spain, in an oral presentation on Saturday, September 9 from 3-3:15 pm CEST (Location: Madrid Auditorium) (Abstract #1214O).

"The updated results of the ECHO-202 trial support earlier published findings, and continue to suggest that the novel immunotherapy combination of epacadostat plus KEYTRUDA has the potential to offer a favorable efficacy and safety profile for the treatment of patients with advanced melanoma," said Omid Hamid, M.D., Chief of Translational Research and Immuno-Oncology and Director of Melanoma Therapeutics, The Angeles Clinic and

Research Institute, Los Angeles, California. "Data have shown that combination immunotherapy can offer higher response rates and improved progression-free survival. These results show that this combination has demonstrated increased and durable response rates and improved progression-free survival, compared to what we would expect from KEYTRUDA alone, without sacrificing safety."

### Key Findings from the ECHO-202 (KEYNOTE-037) Melanoma Cohort

Data at ESMO (as of June 9, 2017) show an ORR of 56 percent among all patients with advanced melanoma treated with the combination of epacadostat and KEYTRUDA, with a complete response (CR) in nine patients (14%); partial response (PR) in 26 patients (41%); and stable disease (SD) in 10 patients (16%). Data also show a disease control rate (DCR) of 71 percent (n=45/63). Of the 35 responses to treatment, 30 were ongoing at the time of analysis; the median duration of response was 45 weeks (range: 1+ to 121+).

ECHO-202 Overall Response Rates (ORR), Disease Control Rates (DCR), Durability of Response (DoR), and Progression-Free Survival (PFS) in Advanced Melanoma Cohort			
	All Patients (N=65)	Treatment-Naïve (all epacadostat doses) (N=54)	Treatment-Naïve (epacadostat 100 mg BID) (N=39)
<b>Per-protocol evaluable n (%)<sup>1</sup></b>	n=63	n=53	n=38
<b>ORR</b>	35 (56)	29 (55)	22 (58)
	9 CR (14)	7 CR (13)	3 CR (8)
	26 PR (41)	22 PR (42)	19 PR (50)
	10 SD (16)	9 SD (17)	6 SD (16)
<b>DCR</b>	45 (71)	38 (72)	28 (74)
	18 PD or death (29)	15 PD or death (28)	10 PD or death (26)
	2 not evaluable <sup>2</sup>	1 not evaluable <sup>2</sup>	1 not evaluable <sup>2</sup>
<b>DoR</b>	30/35 responses ongoing	25/29 responses ongoing	20/22 responses ongoing
	Duration of response: <1+ to 121+ weeks	Duration of response: <1+ to 121+ weeks	Duration of response: <1+ to 81+ weeks
	4/5 patients completing study	3/4 patients completing study treatment	1/1 patient completing study treatment maintained

	treatment maintained ongoing response at last follow-up	maintained ongoing response at last follow-up	ongoing response at last follow-up
<b>Median PFS, months (90% CI)</b>	12.4 (6.2, 23.8)	22.8 (6.2, 23.8)	Not yet reached (4.2, NR)
<b>PFS rate, % (90% CI)</b>	6-month: 65 (54, 74)	6-month: 65 (53, 75)	6-month: 64 (49, 76)
	12-month: 52 (40, 63)	12-month: 52 (38, 64)	12-month: 55 (39, 69)
	18-month: 49 (37, 60)	18-month: 52 (38, 64)	18-month: 55 (39, 69)

1. ≥1 post-baseline scan, or discontinuation or death before first post-baseline scan

2. Scan data not documented in the clinical trial database at time of data cutoff

The most common (≥10 percent) all grade treatment-related adverse events (TRAEs) were rash (46 percent), fatigue (43 percent), pruritus (29 percent), and arthralgia (17 percent). Grade ≥3 TRAEs were observed in 20 percent of patients; the most common were increased lipase (6 percent) and rash (5 percent). Four patients (6 percent) discontinued for TRAEs. No treatment-related deaths occurred. The safety profile was consistent with previously reported Phase 1 findings, as well as the Phase 1/2 safety results in other tumor cohorts and pooled safety data from this study. In general, the safety profile of the combination was also consistent with KEYTRUDA (pembrolizumab) monotherapy.

#### About ECHO-202 (KEYNOTE-037)

The ECHO-202 study (NCT02178722) is evaluating the safety and efficacy of epacadostat, Incyte's selective IDO1 enzyme inhibitor, in combination with KEYTRUDA. Patients previously treated with anti-PD-1 or anti-CTLA-4 therapies were excluded from this trial. Enrollment is complete for the Phase 1 dose escalation (epacadostat 25, 50, 100 mg BID + KEYTRUDA 2 mg/kg IV Q3W and epacadostat 300 mg BID + KEYTRUDA 200 mg IV Q3W) and Phase 1 dose expansion (epacadostat 50, 100, and 300 mg BID + KEYTRUDA 200 mg IV Q3W) portions of the trial. For more information about ECHO-202, visit <https://clinicaltrials.gov/ct2/show/NCT02178722>.

#### About ECHO

The ECHO clinical trial program was established to investigate the efficacy and safety of epacadostat as a core component of combination therapy in oncology. Ongoing Phase 1 and Phase 2 studies are evaluating epacadostat in combination with PD-1 and PD-L1 inhibitors in a broad range of solid tumor types as well as hematological malignancies. ECHO-301 (NCT02752074), a Phase 3 randomized, double-blind, placebo-controlled study investigating KEYTRUDA in combination with epacadostat or placebo for the treatment of patients with unresectable or metastatic melanoma, is also ongoing and fully recruited. For more information about the ECHO clinical trial program, visit [www.ECHOclinicalTrials.com](http://www.ECHOclinicalTrials.com).

#### About Epacadostat (INCB024360)

The immunosuppressive effects of indoleamine 2,3-dioxygenase 1 (IDO1) enzyme activity on the tumor microenvironment help cancer cells evade immunosurveillance. Epacadostat is an investigational, highly potent and selective oral inhibitor of the IDO1 enzyme. In single-arm studies, the combination of epacadostat and immune checkpoint inhibitors has shown proof-of-concept in patients with unresectable or metastatic melanoma, non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck and bladder cancer. In these studies, epacadostat combined with the CTLA-4 inhibitor ipilimumab or the PD-1 inhibitors KEYTRUDA or nivolumab improved response rates compared with studies of the immune checkpoint inhibitors alone.

#### Incyte Conference Call Information

Incyte will host an investor conference call and webcast at 17:00 CET (11:00 a.m. ET) on 9 September 2017—the call and webcast can be accessed via the Events and Presentations tab of the Investor section of [www.incyte.com](http://www.incyte.com).

To access the conference call on Saturday 9 September 2017, please dial 877-407-3042 for domestic callers or +1-201-389-0864 for international callers. When prompted, provide the conference identification number, 13667084.

If you are unable to participate, a replay of the conference call will be available for 30 days. The replay dial-in number for the United States is 877-660-6853 and the dial-in number for international callers is +1-201-612-7415. To access the replay you will need the conference identification number, 13667084.

#### About KEYTRUDA® (pembrolizumab) Injection 100mg

KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Studies of KEYTRUDA (pembrolizumab) – from the largest immuno-oncology program in the industry with more than 550 trials – include a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand factors that predict a patient's likelihood of benefiting from treatment with KEYTRUDA, including the exploration of several different biomarkers across a broad range of tumors.

#### KEYTRUDA (pembrolizumab) Indications and Dosing

##### Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

#### *Lung Cancer*

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS)  $\geq 50\%$ ] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, as a single agent, is also indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS  $\geq 1\%$ ) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

In metastatic NSCLC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

When administering KEYTRUDA in combination with chemotherapy, KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

#### *Head and Neck Cancer*

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In HNSCC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

#### *Classical Hodgkin Lymphoma*

KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In adults with cHL, KEYTRUDA (pembrolizumab) is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression. In pediatric patients with cHL, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

#### *Urothelial Carcinoma*

KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In locally advanced or metastatic urothelial carcinoma, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

#### *Microsatellite Instability-High (MSI-H) Cancer*

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

- solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
- colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

In adult patients with MSI-H cancer, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. In pediatric patients with MSI-H cancer, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

#### **Selected Important Safety Information for KEYTRUDA® (pembrolizumab)**

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected

pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

KEYTRUDA (pembrolizumab) can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%) colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%) hepatitis. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3 or 4 hypophysitis.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in patients with HNSCC, occurring in 28 (15%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (<0.1%) nephritis. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA (pembrolizumab) for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Immune-mediated rashes, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid can occur. Monitor patients for suspected severe skin reactions and based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids. For signs and symptoms of SJS or TEN, withhold KEYTRUDA and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue KEYTRUDA.

KEYTRUDA can cause other clinically important immune-mediated adverse reactions. These immune-mediated reactions may occur in any organ system. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA (pembrolizumab) and administer corticosteroids. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following corticosteroid taper. Permanently discontinue KEYTRUDA for any Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

The following clinically significant immune-mediated adverse reactions occurred in less than 1% (unless otherwise indicated) of 2799 patients: arthritis (1.5%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma. In addition, myelitis and myocarditis were reported in other clinical trials, including classical Hodgkin lymphoma, and postmarketing use.

Solid organ transplant rejection has been reported in postmarketing use of KEYTRUDA. Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients. Consider the benefit of treatment with KEYTRUDA vs the risk of possible organ rejection in these patients.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for signs and symptoms of infusion-related reactions, including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) after being treated with KEYTRUDA. Of 23 patients with cHL who proceeded to allogeneic HSCT after treatment with KEYTRUDA on any trial, 6 patients (26%) developed graft-versus-host-disease (GVHD), one of which was fatal, and 2 patients (9%) developed severe hepatic veno-occlusive disease (VOD) after reduced-intensity conditioning, one of which was fatal. Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor–blocking antibody before transplantation. 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.

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polyneuropathy (0.4%), and cardiac failure (0.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 21% of patients; the most common ( $\geq 1\%$ ) was diarrhea (2.5%). The most common adverse reactions with KEYTRUDA vs ipilimumab were fatigue (28% vs 28%), diarrhea (26% with KEYTRUDA

(pembrolizumab)), rash (24% vs 23%), and nausea (21% with KEYTRUDA). Corresponding incidence rates are listed for ipilimumab only for those adverse reactions that occurred at the same or lower rate than with KEYTRUDA.

KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common ( $\geq 1\%$ ) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and pneumonitis (1%). The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

When KEYTRUDA was administered in combination with carboplatin and pemetrexed (carbo/pem), KEYTRUDA was discontinued in 10% of 59 patients. The most common adverse reaction resulting in discontinuation of KEYTRUDA ( $\geq 2\%$ ) was acute kidney injury (3.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 39% of patients; the most common ( $\geq 2\%$ ) were fatigue (8%), neutrophil count decreased (8%), anemia (5%), dyspnea (3.4%), and pneumonitis (3.4%). The most common adverse reactions ( $\geq 20\%$ ) with KEYTRUDA compared to carbo/pem alone were fatigue (71% vs 50%), nausea (68% vs 56%), constipation (51% vs 37%), rash (42% vs 21%), vomiting (39% vs 27%), dyspnea (39% vs 21%), diarrhea (37% vs 23%), decreased appetite (31% vs 23%), headache (31% vs 16%), cough (24% vs 18%), dizziness (24% vs 16%), insomnia (24% vs 15%), pruritus (24% vs 4.8%), peripheral edema (22% vs 18%), dysgeusia (20% vs 11%), alopecia (20% vs 3.2%), upper respiratory tract infection (20% vs 3.2%), and arthralgia (15% vs 24%). This study was not designed to demonstrate a statistically significant difference in adverse reaction rates for KEYTRUDA as compared to carbo/pem alone for any specified adverse reaction.

KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with HNSCC. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (reported in at least 20% of patients) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC were generally similar to those occurring in patients with melanoma or NSCLC, with the exception of increased incidences of facial edema (10% all Grades; 2.1% Grades 3 or 4) and new or worsening hypothyroidism.

KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL, and treatment was interrupted due to adverse reactions in 26% of patients. Fifteen percent (15%) of patients had an adverse reaction requiring systemic corticosteroid therapy. Serious adverse reactions occurred in 16% of patients. The most frequent serious adverse reactions ( $\geq 1\%$ ) included pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; one from GVHD after subsequent allogeneic HSCT and one from septic shock. The most common adverse reactions (occurring in  $\geq 20\%$  of patients) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).

In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (in  $\geq 20\%$  of patients) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%). Eighteen patients (5%) died from causes other than disease progression. Five patients (1.4%) who were treated with KEYTRUDA experienced sepsis which led to death, and 3 patients (0.8%) experienced pneumonia which led to death. Adverse reactions leading to interruption of KEYTRUDA (pembrolizumab) occurred in 22% of patients; the most common ( $\geq 1\%$ ) were liver enzyme increase, diarrhea, urinary tract infection, acute kidney injury, fatigue, joint pain, and pneumonia. Serious adverse reactions occurred in 42% of patients, the most frequent ( $\geq 2\%$ ) of which were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis.

In KEYNOTE-045, KEYTRUDA was discontinued due to adverse reactions in 8% of 266 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.9%). Adverse reactions leading to interruption of KEYTRUDA occurred in 20% of patients; the most common ( $\geq 1\%$ ) were urinary tract infection (1.5%), diarrhea (1.5%), and colitis (1.1%). The most common adverse reactions (20%) in patients who received KEYTRUDA vs those who received chemotherapy were fatigue (38% vs 56%), musculoskeletal pain (32% vs 27%), pruritus (23% vs 6%), decreased appetite (21% vs 21%), nausea (21% vs 29%), and rash (20% vs 13%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients, the most frequent ( $\geq 2\%$ ) of which were urinary tract infection, pneumonia, anemia, and pneumonitis.

There is limited experience in pediatric patients. Efficacy for pediatric patients was extrapolated from the results in the adult cHL population. In a study of 40 pediatric patients with advanced melanoma, PD-L1–positive advanced, relapsed, or refractory solid tumors or lymphoma, patients were treated with KEYTRUDA for a median of 43 days (range 1-414 days), with 24 patients (60%) receiving treatment for 42 days or more. The safety profile in pediatric patients was similar to that seen in adults treated with KEYTRUDA. Toxicities that occurred at a higher rate ( $\geq 15\%$  difference) in these patients when compared to adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), hypertransaminasemia (28%), and hyponatremia (18%).

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

### About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit the Company's website at [www.incyte.com](http://www.incyte.com).

Follow @Incyte on Twitter at <https://twitter.com/Incyte>.

### About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

## Forward-Looking Statement of Incyte Corporation

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding whether the combination of epacadostat plus KEYTRUDA will offer a safe and effective treatment for patients with advanced melanoma and the phase 3 trial of epacadostat in combination with KEYTRUDA for the treatment of melanoma, contain predictions, estimates and other forward-looking statements. These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments and the risks related to the efficacy or safety of the Company's development pipeline, the results of further research and development, the high degree of risk and uncertainty associated with drug development, clinical trials and regulatory approval processes, other market or economic factors and competitive and technological advances; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission, including its Form 10-Q for the quarter ended June 30, 2017. Incyte disclaims any intent or obligation to update these forward-looking statements.

## Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2016 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ( [www.sec.gov](http://www.sec.gov) ).

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf) and Patient Information/Medication Guide for KEYTRUDA at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_mg.pdf](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf).

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