Incyte and Merck Expand Clinical Collaboration to Include Phase 3 Study Investigating the Combination of Epacadostat with Keytruda® (pembrolizumab) as First-line Treatment for Advanced Melanoma

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Pivotal study to evaluate Incyte's IDO1 inhibitor in combination with Merck's anti-PD-1 therapy in patients with advanced or metastatic melanoma

WILMINGTON, Del. & KENILWORTH, N.J.--(BUSINESS WIRE)--Oct. 13, 2015-- Incyte Corporation (Nasdaq: INCY) and Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced the expansion of the companies' ongoing clinical collaboration to include a Phase 3 study evaluating the combination of epacadostat, Incyte's investigational selective IDO1 inhibitor, with Keytruda ® (pembrolizumab), Merck's anti-PD-1 therapy, as first-line treatment for patients with advanced or metastatic melanoma. The Phase 3 study, which is expected to begin in the first half of 2016, will be co-funded by Incyte and Merck.

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"We are very pleased to expand our collaboration with Merck and to move the clinical development program for epacadostat in combination with Keytruda into Phase 3," said Hervé Hoppenot, President and Chief Executive Officer of Incyte. "We believe the combination of these two immunotherapies shows promise and, if successfully developed, may help to improve clinical outcomes for patients with metastatic melanoma."

"The initiation of this large Phase 3 study with Incyte in the first-line advanced melanoma treatment setting is an important addition to our robust immunotherapy clinical development program for Keytruda," said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. "We continue to explore the benefit that Keytruda brings to patients suffering from advanced melanoma when used alone, and we are pleased to be able to add this important combination study with epacadostat to our Keytruda development program."

Under the terms of the agreement Incyte and Merck have also agreed, for a period of two years, not to initiate new pivotal studies of an IDO1 inhibitor in combination with a PD-1/PD-L1 antagonist as first-line therapy in advanced or metastatic melanoma with any third party. During this time, the companies will each offer the other the opportunity to collaborate on any new pivotal study involving an IDO1 inhibitor in combination with a PD-1/PD-L1 antagonist for types of melanoma and lines of therapy outside of the current collaboration agreement.

The agreement is between Incyte and certain subsidiaries and Merck through its subsidiaries.

Epacadostat and Keytruda are part of a class of cancer treatments known as immunotherapies that are designed to enhance the body's own defenses in fighting cancer; the two therapies target distinct regulatory components of the immune system. IDO1 is an immunosuppressive enzyme that has been shown to induce regulatory T cell generation and activation, and allow tumors to escape immune surveillance. Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. Preclinical evidence suggests that the combination of these two agents may lead to an enhanced anti-tumor immune response compared with either agent alone.

Safety and efficacy data from the ongoing Phase 1/2 study evaluating the combination of epacadostat with Keytruda in patients with advanced malignancies is scheduled to be highlighted as a late-breaking oral presentation (Abstract #142) at the upcoming Society for Immunotherapy of Cancer 30th Anniversary Annual Meeting & Associated Programs, November 4–8, 2015 at the Gaylord National Resort & Convention Center in National Harbor, MD.

Metastatic Melanoma

Melanoma, the most serious form of skin cancer, strikes adults of all ages and accounts for approximately five percent of all new cases of cancer in the United States each year. The number of new cases of melanoma continues to rise by almost three percent each year which translates to 76,000 new cases yearly in the U.S. alone.[1] The 5-year survival rate for late-stage or metastatic disease is 15 percent.[2]

About Epacadostat (INCB024360)

Indoleamine 2,3-dioxygenase 1 (IDO1) is an immunosuppressive enzyme that has been shown to induce regulatory T cell generation and activation, and allow tumors to escape immune surveillance. Epacadostat is an orally bioavailable small molecule inhibitor of IDO1 that has nanomolar potency in both biochemical and cellular assays and has demonstrated potent activity in enhancing T lymphocyte, dendritic cell and natural killer cell responses in vitro, with a high degree of selectivity. Epacadostat has shown proof-of-concept clinical data in patients with unresectable or metastatic melanoma in combination with the CTLA-4 inhibitor ipilimumab, and is currently in four proof-of-concept clinical trials with PD-1 and PD-L1 immune checkpoint inhibitors in a variety of cancer histologies.

About Keytruda® (pembrolizumab) Injection 100mg In Melanoma

Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. By binding to the PD-1 receptor and blocking the interaction with the receptor ligands, Keytruda releases the PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. Keytruda is indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Selected Important Safety Information for Keytruda in Melanoma Trials

Pneumonitis occurred in 12 (2.9%) of 411 patients, including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively, receiving Keytruda. 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 pneumonitis.

Colitis (including microscopic colitis) occurred in 4 (1%) of 411 patients, including Grade 2 or 3 cases in 1 (0.2%) and 2 (0.5%) patients, respectively, receiving Keytruda. 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.

Hepatitis (including autoimmune hepatitis) occurred in 2 (0.5%) of 411 patients, including a Grade 4 case in 1 (0.2%) patient, receiving Keytruda. 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.

Hypophysitis occurred in 2 (0.5%) of 411 patients, including a Grade 2 case in 1 and a Grade 4 case in 1 (0.2% each) patient, receiving Keytruda. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids for Grade 2 or greater hypophysitis. Withhold Keytruda for Grade 2; withhold or discontinue for Grade 3; and permanently discontinue Keytruda for Grade 4 hypophysitis.

Hyperthyroidism occurred in 5 (1.2%) of 411 patients, including Grade 2 or 3 cases in 2 (0.5%) and 1 (0.2%) patients, respectively, receiving Keytruda. Hypothyroidism occurred in 34 (8.3%) of 411 patients, including a Grade 3 case in 1 (0.2%) patient, receiving Keytruda. Thyroid disorders can occur at any time during treatment. 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 corticosteroids for Grade 3 or greater hyperthyroidism. Withhold Keytruda for Grade 3; permanently discontinue Keytruda for Grade 4 hyperthyroidism. Isolated hypothyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.

Type 1 diabetes mellitus, including diabetic ketoacidosis, has occurred in patients receiving Keytruda. Monitor patients for hyperglycemia and other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold Keytruda in cases of severe hyperglycemia until metabolic control is achieved.

Nephritis occurred in 3 (0.7%) patients, consisting of one case of Grade 2 autoimmune nephritis (0.2%) and two cases of interstitial nephritis with renal failure (0.5%), one Grade 3 and one Grade 4. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold Keytruda for Grade 2; permanently discontinue Keytruda for Grade 3 or 4 nephritis.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant immune-mediated adverse reactions occurred in patients treated with Keytruda: exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, severe dermatitis including bullous pemphigoid, myasthenic syndrome, optic neuritis, and rhabdomyolysis.

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 and administer corticosteroids. Upon improvement of the adverse reaction to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Restart Keytruda if the adverse reaction remains at Grade 1 or less. Permanently discontinue Keytruda for any severe or Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

Infusion-related reactions, including severe and life-threatening reactions, have occurred in patients receiving Keytruda. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For severe or life-threatening reactions, stop infusion and permanently discontinue Keytruda.

Based on its mechanism of action, Keytruda may 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.

Keytruda was discontinued for adverse reactions in 9% of 411 patients. Adverse reactions, reported in at least two patients, that led to discontinuation of Keytruda were: pneumonitis, renal failure, and pain. Serious adverse reactions occurred in 36% of patients. The most frequent serious adverse reactions, reported in 2% or more of patients, were renal failure, dyspnea, pneumonia, and cellulitis.

The most common adverse reactions (reported in at least 20% of patients) were fatigue (47%), cough (30%), nausea (30%), pruritus (30%), rash (29%), decreased appetite (26%), constipation (21%), arthralgia (20%), and diarrhea (20%).

No formal pharmacokinetic drug interaction studies have been conducted with Keytruda.

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.

The recommended dose of Keytruda (pembrolizumab) is 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity. No formal pharmacokinetic drug interaction studies have been conducted with Keytruda. 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. Safety and effectiveness of Keytruda have not been established in pediatric patients.

About Incyte

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics, primarily for oncology. For additional information on Incyte, please visit the Company's website at www.incyte.com.

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck Oncology, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in immuno-oncology and we are accelerating every step in the journey – from lab to clinic – to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside of the United States and Canada. 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 healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook and YouTube.

Forward-Looking Statement of Incyte

Except for the historical information set forth herein, the matters set forth in this press release, including without limitation statements with respect to the planned commencement of the Phase 3 trial for epacadostat in combination with pembrolizumab for advanced or metastatic melanoma, the efficacy of such trial and the effect such trial may have on patient outcomes, the planned presentation of safety and efficacy data from the ongoing Phase 1/2 study for epacadostat in combination with Keytruda, and the parties' future obligations under the expanded collaboration agreement, contain predictions and estimates and are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on Incyte's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including the high degree of risk associated with drug development, results of further research and development, unanticipated delays, other market or economic factors and technological advances, regulatory approval of the transaction and other risks detailed from time to time in Incyte's filings with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended June 30, 2015. Incyte disclaims any intent or obligation to update these forward-looking statements.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, NJ, USA

This news release of Merck & Co., Inc., Kenilworth, NJ, USA (the "Company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States 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 healthcare legislation in the United States and internationally; global trends toward healthcare 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 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 2014 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).

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf and the Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf

[1] Siegel R, Naishadham MA, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. Jan- 2012;62:10-29.

[2]American Cancer Society. Melanoma Skin Cancer. Atlanta, GA: American Cancer Society (ACS); 2015. http://www.cancer.org/cancer/skincancer-melanoma/index. Accessed May 13, 2015.

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