Merck and DNAtrix Announce Phase 2 Immuno-Oncology Collaboration in Patients with Aggressive Form of Brain Cancer

KENILWORTH, N.J. & HOUSTON--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, and DNAtrix today announced they have entered into an oncology clinical study collaboration to evaluate the efficacy and safety of DNX-2401, DNAtrix's oncolytic immunotherapy, in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, in a Phase 2, multi-centered study of patients with recurrent glioblastoma, the most aggressive form of brain cancer for which there is no cure.

DNX-2401 is a conditionally replicative oncolytic adenovirus designed to specifically target cells defective in the Retinoblastoma (Rb) pathway, which is present in many cancers. Several DNX-2401 clinical studies have demonstrated a favorable safety profile and strong tumor-killing potential in patients with recurrent glioblastoma. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 (programmed death receptor-1) and its ligands, PD-L1 and PD-L2. KEYTRUDA is currently approved in the United States for certain types of advanced metastatic melanoma.

"We are excited to enter into this important collaboration with Merck as we investigate the potential anti-tumor effect that combining our two immunotherapies – DNX-2401 and KEYTRUDA – may offer patients with this aggressive disease," said Frank Tufaro, Ph.D., chief executive officer of DNAtrix.

"The collaboration with DNAtrix further strengthens our efforts to progress the field of immuno-oncology and identify potential combinations that will significantly advance the care of people with cancers for which there have been few advancements," said Dr. Eric Rubin, vice president and therapeutic area head, oncology early-stage development, Merck Research Laboratories. "We look forward to studying the potential synergistic effects that combining DNX-2401 and KEYTRUDA could have in the treatment of patients with recurrent glioblastoma."

The agreement is between DNAtrix and Merck, through a subsidiary. Additional details of the collaboration were not disclosed.

About Glioblastoma

Glioblastoma is a type of glioma, which are tumors that arise from glial cells, or supportive brain cells that help to keep neurons in place and functioning well. Glioblastoma is highly malignant because the cells reproduce quickly and are supported by a large network of blood vessels. While glioblastoma rarely spreads elsewhere in the body, these tumors arise from normal brain cells, so it is easy for them to invade and live within normal brain tissue. Glioblastoma represents 17 percent of all primary brain tumors and 54 percent of all gliomas.

About DNX-2401
DNX-2401 is an investigational oncolytic immunotherapy designed to treat high grade gliomas. Upon tumor injection, DNX-2401 sets off a chain reaction of tumor cell killing by selectively replicating within glioma cells (but not normal cells), causing tumor destruction and further spread of the oncolytic virus to adjacent tumor cells. This process can also trigger an anti-tumor immune response. DNX-2401 is currently being investigated in several clinical studies and has been well tolerated in all settings. Compelling results from Phase I clinical studies in recurrent glioblastoma indicate that DNX-2401 can (1) replicate in human brain tumors for a period of weeks to months (2) trigger immune cell infiltration into the tumor (3) cause ongoing tumor destruction detectable by MRI and (4) induce durable responses to therapy. In these studies, patient survival has been prolonged in a subset of patients, including in those achieving a complete response.

About KEYTRUDA® (pembrolizumab)
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
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%).

The recommended dose of KEYTRUDA 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 DNAtrix
DNAtrix is a privately held, clinical stage, biotechnology company developing virus-driven immunotherapies for cancer. DNAtrix's lead product, DNX-2401, is a conditionally replicative oncolytic virus being studied in clinical trials for recurrent glioblastoma, an incurable brain cancer. The company is backed by Morningside Ventures and Mercury Fund, and has been awarded a grant from the Cancer Prevention and Research Institute of Texas (CPRIT). For more information, please visit the company website at http://www.dnatrix.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 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

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