# New Trial Initiated Evaluating Amgen's Talimogene Laherparepvec In Combination With Merck's Anti-PD-1 Therapy KEYTRUDA® (Pembrolizumab) For Advanced Melanoma

December 8, 2014

**Study is the First to Evaluate Investigational Combination of an Oncolytic Immunotherapy and Anti-PD-1 Therapy**

THOUSAND OAKS, Calif., Dec. 8, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced the initiation of a trial of talimogene laherparepvec, an investigational oncolytic immunotherapy, in combination with an investigational use of Merck's U.S. Food and Drug Administration (FDA) approved, anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) in patients with regionally or distantly metastatic melanoma. The trial has enrolled its first patient and will evaluate the combination of these two therapies in approximately 110 patients across 35 clinical trial sites in the U.S., Australia and Europe.

"Data from this trial will help us further understand the safety and efficacy that comes from combining two immunotherapeutic agents," said F. Stephen Hodi, M.D., director of the Melanoma Center and the Center for Immuno-Oncology at Dana-Farber Cancer Institute and Steering Committee Chair for this study. "Talimogene laherparepvec is designed to promote tumor antigen release and presentation to initiate an anti-tumor immune response, which may be complementary to KEYTRUDA's role in releasing PD-1 pathway-mediated inhibition of anti-tumor immune responses. Antigen release and presentation is a fundamental step required for mounting a systemic effect against melanoma, and we think there is a strong rationale for combining the oncolytic immunotherapy talimogene laherparepvec with the immune checkpoint inhibitor KEYTRUDA."

"This new trial underscores our commitment to researching different treatment approaches for patients with this aggressive and highly recurrent form of skin cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We are excited to partner with Merck and explore the potential of talimogene laherparepvec and KEYTRUDA. This will also give us insights into talimogene laherparepvec beyond the monotherapy setting, where a Phase 3 trial has shown encouraging results."

"Merck is advancing the study of immuno-oncology combinations with KEYTRUDA across a broad range of malignancies," said Dr. Eric Rubin, vice president, Clinical Development for Oncology, Merck Research Laboratories. "We are pleased to collaborate with Amgen to evaluate the potential of KEYTRUDA and talimogene laherparepvec as a combination regimen for the treatment of advanced melanoma."

A Biologics License Application has recently been accepted for review by the FDA as has a Marketing Authorization Application in the European Union for talimogene laherparepvec for the treatment of patients with regionally or distantly metastatic melanoma. FDA has set a review goal date under the Prescription Drug User Fee Act (PDUFA) of July 28, 2015.

The regulatory filings included data from more than 400 patients and is based on a global, randomized, open-label Phase 3 trial evaluating the safety and efficacy of intralesional talimogene laherparepvec in patients with stage IIIB, IIIC, or IV melanoma that are not surgically resectable compared to granulocyte-macrophage colony-stimulating factor (GM-CSF). An Amgen-sponsored expanded access protocol (EAP) is currently active for qualified patients with unresected, stage IIIB to IV melanoma who are not eligible for or who cannot access ongoing talimogene laherparepvec trials.

**About the Combination Trial**

The multicenter, open-label clinical trial is designed to evaluate the safety of talimogene laherparepvec in combination with KEYTRUDA, as well as the efficacy of this combination versus KEYTRUDA alone and following progression after treatment with KEYTRUDA alone.

The study will be conducted in two phases:

- Phase 1 will determine the safety and tolerability of talimogene laherparepvec in combination with KEYTRUDA in patients with previously untreated, unresected, stage IIIB to IVM1c melanoma.
- The randomized phase will further evaluate the safety and efficacy of talimogene laherparepvec in combination with KEYTRUDA.

**About Talimogene Laherparepvec**

Talimogene laherparepvec is an investigational oncolytic immunotherapy designed to selectively replicate in tumors (but not normal tissue) and to initiate an immune response to target cancer cells that have metastasized. Talimogene laherparepvec was designed to work in two important and complementary ways. First, it is injected directly into tumors where it replicates inside the tumor's cells causing the cell to rupture and die in a process called lysis. Then, the rupture of the cancer cells can release tumor-derived antigens, along with GM-CSF, that can stimulate a system-wide immune response where white blood cells are able to seek out and target cancer that has spread throughout the body.

Amgen has initiated a comprehensive clinical development program for talimogene laherparepvec in metastatic melanoma, which includes combination studies with checkpoint inhibitors in patients with late-stage disease and monotherapy prior to surgery (neoadjuvant) in patients with resectable disease. Additionally, based on its mechanism of action, talimogene laherparepvec has the potential to be studied in a variety of solid tumor types.

**Access to Investigational Medicines**

To serve patients, Amgen engages in clinical research with the goal of obtaining regulatory approval of its products. Clinical trials allow Amgen to evaluate investigational new treatments in volunteers in order to generate the safety and efficacy information needed to obtain approval of those treatments and make them available to the broader patient population. Outside of a clinical trial, access to Amgen's investigational products would be considered under limited circumstances and as permitted by applicable law. More information can be found here on the Amgen website.

**About Melanoma**

Melanoma is a type of skin cancer that is characterized by the uncontrolled growth of melanocytes, which are the cells responsible for providing the pigment to skin.[1] Melanoma is the most aggressive and serious form of skin cancer. Currently, 132,000 melanoma cases occur globally each year.[2] In

the U.S., while melanoma accounts for less than five percent of skin cancer cases, it causes the most skin cancer deaths.[3] The number of new cases of melanoma in the U.S. has been increasing for the last 30 years.[3]

Melanoma is considered to be advanced when it has spread, or metastasized, from the origin site to deeper parts of the skin or other organs such as the lymph nodes, lungs or other parts of the body distant from the primary tumor site.[4]

**About Amgen**
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be the world's largest independent biotechnology company, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

**Forward-Looking Statements**
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen, we or us) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of Dec. 8, 2014, and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us and our partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products (including products of our wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to integrate the operations of companies we have acquired may not be successful. Cost savings initiatives may result in us incurring impairment or other related charges on our assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plans. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase common stock.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

CONTACT: Amgen Thousand Oaks
Kristen Davis, 805-447-3008 (media)
Arvind Sood, 805-447-1060 (investors)

**References:**
1. National Cancer Institute, National Institute of Health, U.S. Dept. of Health and Human Services. *What You Need to Know About* Melanoma and

Other Skin Cancers. June 2010.http://www.cancer.gov/cancertopics/wyntk/skin. Accessed July 18, 2014.
2. World Health Organization. Ultraviolet radiation and the INTERSUN Programme. http://www.who.int/uv/faq/skincancer/en/index1.html. Accessed July 18, 2014.
3. Melanoma skin cancer overview. American Cancer Society website. http://www.cancer.org/acs/groups/cid/documents/webcontent/003063-pdf.pdf Accessed July 18, 2014.
4. American Cancer Society. Melanoma Skin Cancer. http://www.cancer.org/acs/groups/cid/documents/webcontent/003120-pdf.pdf Accessed July 18, 2014.

Logo - http://photos.prnewswire.com/prnh/20081015/AMGENLOGO

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/new-trial-initiated-evaluating-amgens-talimogene-laherparepvec-in-combination-with-mercks-anti-pd-1-therapy-keytruda-pembrolizumab-for-advanced-melanoma-300006422.html

SOURCE Amgen