# Amgen Receives CHMP Positive Opinion For IMLYGIC™ (Talimogene Laherparepvec)

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**IMLYGIC is First Oncolytic Immunotherapy to Demonstrate Therapeutic Benefit for Patients With Advanced Melanoma**

THOUSAND OAKS, Calif., Oct. 23, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Committee for Medicinal Products for Human Use (CHMP), the scientific committee of the European Medicines Agency (EMA), has adopted a positive opinion recommending that IMLYGIC™ (talimogene laherparepvec) be granted approval for the treatment of adults with unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease. If approved by the European Commission, IMLYGIC would be the first in a class of novel agents known as oncolytic immunotherapies.

IMLYGIC, administered via intralesional injection, is designed to cause the death of tumor cells and to initiate an anti-tumor immune response.

"We are pleased that IMLYGIC has received a positive opinion from the CHMP, and if approved by the European Commission, we look forward to continuing to work with European regulatory authorities to bring this innovative therapy to patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Metastatic melanoma continues to be one of the most difficult-to-treat cancers, often requiring the use of multiple treatment modalities. Despite recent advances, the five-year survival rate for patients who cannot be cured with surgery remains unacceptably low, demonstrating the critical need for additional approaches to control this disease."

The positive CHMP opinion was based on a global, randomized, open-label Phase 3 trial evaluating the safety and efficacy of IMLYGIC in patients with Stage IIIB, IIIC or IV melanoma when resection was not recommended compared to granulocyte-macrophage colony-stimulating factor (GM-CSF). In the 436-patient study, IMLYGIC significantly improved durable response rate (DRR), the primary endpoint of the trial, in the intent-to-treat population. DRR is defined as the percent of patients with complete response (CR) or partial response (PR) maintained continuously for a minimum of six months. A key secondary endpoint was overall survival (OS). The positive CHMP opinion reflects subgroup analyses where the effect on OS was largest in patients with unresectable melanoma that has not spread beyond the skin or lymph nodes.

The most commonly reported treatment-related adverse events were fatigue, chills, pyrexia, nausea, influenza-like illness and injection-site pain. Overall, 98 percent of these adverse reactions reported were mild or moderate in severity. The most common grade 3 or higher adverse reaction was cellulitis.

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, and remains a significant public health concern in the European Union (EU).[2,3] In 2012, it was estimated that there were 56,000 new cases of melanoma in France, Italy, Spain, Germany and the U.K. causing nearly 9,500 deaths.[4,5]

Following this CHMP opinion, Amgen expects a decision on the Marketing Authorization from the European Commission in the coming months. IMLYGIC is also under review by the U.S. Food and Drug Administration.

**About IMLYGIC (talimogene laherparepvec) in the EU**

IMLYGIC is an oncolytic immunotherapy that is derived from HSV-1, which is commonly called the cold sore virus. IMLYGIC has been modified to replicate within tumors and to produce the immune stimulatory protein human GM-CSF. IMLYGIC causes the death of tumor cells and the release of tumor-derived antigens. It is thought that, together with GM-CSF, it will promote a systemic anti-tumor immune response and an effector T cell response.

**About IMLYGIC (talimogene laherparepvec) in the U.S.**

IMLYGIC is a genetically modified herpes simplex type 1 virus that is injected directly into tumors. IMLYGIC replicates inside tumor cells and produces GM-CSF, an immunostimulatory protein. IMLYGIC then causes the cell to rupture and die in a process called lysis. The rupture of the cancer cells causes the release of tumor-derived antigens, which together with virally derived GM-CSF may help to promote an anti-tumor immune response. However, the exact mechanism of action is unknown.

**About Amgen's Immuno-Oncology Focused Partnerships**

Amgen has in place a comprehensive clinical development program investigating oncolytic immunotherapies for their potential in melanoma and in a variety of other cancers.

Amgen's recent immuno-oncology focused partnerships include:

- A collaboration with Merck on developing IMLYGIC and KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, in melanoma and squamous cell cancer of the head and neck.
- A collaboration with Roche on a Phase 1b study to evaluate the safety and efficacy of IMLYGIC in combination with Roche's investigational anti-PDL1 therapy, atezolizumab (also known as MPDL3280A), in patients with triple-negative breast cancer and colorectal cancer with liver metastases.
- A strategic research collaboration and license agreement to develop and commercialize the next generation of novel Chimeric Antigen Receptor (CAR) T cell immunotherapies with Kite Pharma.
- A research collaborative agreement focusing on Amgen's bispecific T cell engager (BiTE®) antibody constructs with MD Anderson's Moon Shots Program.

- A research and license agreement with Xencor to develop and commercialize novel therapeutics in the areas of cancer immunotherapy and inflammation. The research collaboration brings together Amgen's capabilities in target discovery and protein therapeutics with Xencor's XmAb® bispecific technology platform.

**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 one of the world's leading independent biotechnology companies, 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.

**About Amgen's Commitment to Oncology**

Amgen Oncology is committed to helping patients take on some of the toughest cancers, such as those that have been resistant to drugs, those that progress rapidly through the body and those where limited treatment options exist. Amgen's supportive care treatments help patients combat certain side effects of strong chemotherapy, and our targeted medicines and immunotherapies focus on more than a dozen different malignances, ranging from blood cancers to solid tumors. With decades of experience providing treatments for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

**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 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 Oct. 23, 2015, 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 Amgen and its partners routinely obtain patents for 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. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our ongoing restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

The scientific information discussed in this news release related to our product candidates is limited to the European Union. Such product candidates

are not approved by the U.S. Food and Drug Administration or the European Commission, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

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