FDA Approves IMLYGIC™ (Talimogene Laherparepvec) As First Oncolytic Viral Therapy In The US

October 27, 2015

IMLYGIC Indicated for the Local Treatment of Unresectable Cutaneous, Subcutaneous and Nodal Lesions in Patients With Melanoma Recurrent After Initial Surgery

Patients Treated With IMLYGIC Achieved a Significant Increase in Durable Response Rate in Pivotal Study

THOUSAND OAKS, Calif., Oct. 27, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved the Biologics License Application for IMLYGIC ™(talimogene laherparepvec), a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous and nodal lesions in patients with melanoma recurrent after initial surgery. IMLYGIC has not been shown to improve overall survival or have an effect on visceral metastases. IMLYGIC is the first oncolytic viral therapy approved by the FDA based on therapeutic benefit demonstrated in a pivotal study.[1-3]

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IMLYGIC is a genetically modified herpes simplex virus type 1 designed to replicate within tumors and produce an immunostimulatory protein called granulocyte-macrophage colony-stimulating factor (GM-CSF). IMLYGIC causes cell lysis, or death, which ruptures tumors, releasing tumor-derived antigens, which along with GM-CSF, may promote an anti-tumor immune response. However, the exact mechanism of action is unknown.

"IMLYGIC is the first clinical and regulatory validation of an oncolytic virus as a therapy, which Amgen is proud to bring to patients with a serious form of skin cancer. Not all melanoma patients currently benefit from available therapies, and IMLYGIC represents an important new option that can provide meaningful durable responses for patients with this aggressive and complex disease," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Immunotherapy is an exciting area for cancer research, and we are currently studying IMLYGIC in combination with other immunotherapies in advanced melanoma and other solid tumors."

"Advanced melanoma remains a complex disease to treat, requiring the use of several modalities over the course of a patient's therapeutic journey," said Howard L. Kaufman, M.D., the principal investigator for the pivotal trial (OPTiM), associate director for Clinical Science at the Rutgers Cancer Institute of New Jersey and president of the Society for Immunotherapy of Cancer. "As an oncolytic viral therapy, IMLYGIC has a unique approach, and provides another option for treating eligible patients with unresectable disease that has recurred after initial surgery."

Metastatic melanoma continues to be one of the most difficult-to-treat cancers because it is often insensitive to chemotherapy, can be highly aggressive and can require several different types of treatment depending on the stage and location of the disease and health of the patient.[4,5] Despite new therapeutic options, additional treatments are needed – particularly for patients with metastatic disease.

Amgen intends to make IMLYGIC available to patients in the U.S. within a week. Amgen anticipates the average cost of IMLYGIC therapy to be approximately $65,000. Given that IMLYGIC represents a novel and first-in-class oncolytic viral therapy, Amgen expects variability of IMLYGIC dosing from patient to patient. Therefore, Amgen intends to work with the healthcare community to implement a program that helps limit the average cost of IMLYGIC therapy to $65,000 for eligible participating institutions.

Amgen is committed to helping clinically appropriate patients access our medicines and will provide assistance for IMLYGIC in the U.S. in the following ways:

- Free medicines through The Safety Net Foundation are available to qualifying individuals with no or limited drug coverage.
- Co-pay coupon program for IMLYGIC through the Amgen FIRST STEP™ Program to help commercially insured patients meet their co-payment obligations; this program has no income requirement. Further information about eligibility requirements can be found at www.amgenfirststep.com.
- Information about independent co-pay assistance foundations that give grants to qualifying patients who have difficulty paying out-of-pocket costs for medicines manufactured from across all of the industry.

For more information, visit www.amgenassistonline.com.

About the OPTiM Study

The approval of IMLYGIC is based on data from Study 005/05, referred to as OPTiM. OPTiM was a Phase 3, multicenter, open-label, randomized clinical trial comparing IMLYGIC to GM-CSF in patients with advanced melanoma (Stage IIIB, IIIC, or IV) that was not surgically resectable. The primary endpoint of the study was durable response rate (DRR), defined as the percent of patients with complete response (CR) or partial response (PR) maintained continuously for a minimum of six months.

OPTiM enrolled 436 patients. In the study, 16.3 percent of patients treated with IMLYGIC achieved a durable response compared to 2.1 percent of patients treated with GM-CSF (p <0.0001). Of the patients who experienced a durable response, 29.1 percent had a durable CR and 70.8 percent had a durable PR. In the study, the median time to response was 4.1 (range: 1.2 to 16.7) months in the IMLYGIC arm.

The most common adverse drug reactions in IMLYGIC treated patients were fatigue, chills, pyrexia, nausea, influenza-like illness and injection site pain. Most adverse reactions reported were mild or moderate in severity and generally resolved within 72 hours. The most common grade 3 or higher adverse reaction was cellulitis.[2]

About IMLYGIC (talimogene laherparepvec)

IMLYGIC is a genetically modified herpes simplex virus type 1 injected directly into tumors where it replicates inside tumors and produces GM-CSF, an immunostimulatory protein. IMLYGIC then causes the tumor to rupture and die in a process called lysis. The rupture of the tumor causes the release of

tumor-derived antigens, which together with virally-derived GM-CSF may promote an anti-tumor immune response. However, the exact mechanism of action is unknown and being further investigated.

Important Safety Information

Contraindications

- Do not administer IMLYGIC ™to immunocompromised patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, AIDS or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy, due to the risk of life-threatening disseminated herpetic infection.
- Do not administer IMLYGIC ™to pregnant patients.

Warnings and Precautions

- **Accidental exposure to IMLYGIC ™** may lead to transmission of IMLYGIC ™and herpetic infection, including during preparation and administration. Health care providers, close contacts, pregnant women, and newborns should avoid direct contact with injected lesions, dressings, or body fluids of treated patients. The affected area in exposed individuals should be cleaned thoroughly with soap and water and/or a disinfectant.
- Caregivers should wear protective gloves when assisting patients in applying or changing occlusive dressings and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant.
- To prevent possible inadvertent transfer of IMLYGIC ™to other areas of the body, patients should be advised to avoid touching or scratching injection sites or occlusive dressings.
- **Herpetic infections:** Herpetic infections (including cold sores and herpetic keratitis) have been reported in IMLYGIC ™treated patients. Disseminated herpetic infection may also occur in immunocompromised patients. Patients who develop suspicious herpes-like lesions should follow standard hygienic practices to prevent viral transmission.
- Patients or close contacts with suspected signs or symptoms of a herpetic infection should contact their health care provider to evaluate the lesions. Suspected herpetic lesions should be reported to Amgen at 1-855-IMLYGIC (1-855-465-9442). Patients or close contacts have the option of follow-up testing for further characterization of the infection.
- IMLYGIC ™is sensitive to acyclovir. Acyclovir or other antiviral agents may interfere with the effectiveness of IMLYGIC ™. Consider the risks and benefits of IMLYGIC ™treatment before administering antiviral agents to manage herpetic infection.
- **Injection Site Complications:** Necrosis or ulceration of tumor tissue may occur during IMLYGIC ™treatment. Cellulitis and systemic bacterial infection have been reported in clinical studies. Careful wound care and infection precautions are recommended, particularly if tissue necrosis results in open wounds.
- Impaired healing at the injection site has been reported. IMLYGIC ™may increase the risk of impaired healing in patients with underlying risk factors (e.g., previous radiation at the injection site or lesions in poorly vascularized areas). If there is persistent infection or delayed healing of the injection site, consider the risks and benefits of continuing treatment.
- **Immune-Mediated events** including glomerulonephritis, vasculitis, pneumonitis, worsening psoriasis, and vitiligo have been reported in patients treated with IMLYGIC ™. Consider the risks and benefits of IMLYGIC ™before initiating treatment in patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.
- **Plasmacytoma at Injection Site:** Plasmacytoma in proximity to the injection site has been reported in a patient with smoldering multiple myeloma after IMLYGIC ™administration in a clinical study. Consider the risks and benefits of IMLYGIC ™in patients with multiple myeloma or in whom plasmacytoma develops during treatment.

Adverse Reactions

- The most commonly reported adverse drug reactions (≥ 25%) in IMLYGIC ™-treated patients were fatigue, chills, pyrexia, nausea, influenza-like illness, and injection site pain. Pyrexia, chills, and influenza-like illness can occur at any time during IMLYGIC ™treatment, but were more frequent during the first 3 months of treatment.
- The most common Grade 3 or higher adverse reaction was cellulitis.

Please see full Prescribing Information, including Medication Guide, for IMLYGIC at www.Amgen.com and www.IMLYGIC.com.

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.

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 Oct. 27, 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 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. 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 our ability to pay a dividend or repurchase common stock.

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