Amgen Presents New Phase 2 Data On IMLYGIC® (Talimogene Laherparepvec) Investigational Combination At ASCO 2017

June 3, 2017

First Randomized Study to Evaluate the Combination of IMLYGIC, an Oncolytic Viral Therapy, With a Checkpoint Inhibitor Data Demonstrate IMLYGIC in Combination With YERVOY® (Ipilimumab) Doubled Objective Response Rate in Unresectable Advanced Melanoma

Responses Not Limited to Injected Lesions; 50 Percent or Higher Reduction in Visceral Lesion Size Occurred More Frequently in Patients in the Combination Arm

THOUSAND OAKS, Calif., June 3, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new data from the Phase 2 '264 study that demonstrated IMLYGIC® (talimogene laherparepvec) in combination with the immune checkpoint inhibitor YERVOY® (ipilimumab)* more than doubled objective response rate (ORR), defined as the proportion of patients with tumor size reduction, compared to YERVOY alone in patients with unresectable stage IIIB-IV melanoma, meeting the primary endpoint of the study. The analysis showed that 38.8 percent of patients treated with IMLYGIC plus YERVOY achieved an objective response versus 18 percent of patients treated with YERVOY alone (odds ratio=2.9, 95 percent CI: 1.5, 5.5; *p*=0.002). Patients in the combination arm also experienced nearly double the complete response rate compared to YERVOY alone (13.3 percent versus 7 percent). The results were presented at the 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO).

"Metastatic melanoma continues to be one of the most difficult-to-treat and aggressive cancers," said Jason Chesney, M.D., '264 study investigator and acting director of the James Graham Brown Cancer Center, University of Louisville, Louisville, Ky. "The results from this study demonstrate the potential of combining the complementary mechanisms of action of an oncolytic viral immunotherapy and a checkpoint inhibitor to enhance anti-tumor effect in patients with advanced melanoma."

Responses were not limited to injected lesions. Among patients with visceral disease treated with IMLYGIC plus YERVOY, 35 percent had a reduction in size of visceral lesions by at least 50 percent. The rate was 14 percent in patients in the YERVOY arm. Patients in the IMLYGIC plus YERVOY arm experienced a median progression-free survival (PFS) of 8.2 months (median follow up 68 weeks) versus 6.4 months in the YERVOY arm. The effect was not statistically significant (HR=0.83, 95 percent CI; *p*=0.35); however, the PFS analysis was not event-driven and is still ongoing, with only approximately 50 percent of PFS events reported at this time.

"Patients with metastatic melanoma are in need of innovative, effective treatment options that can improve response rates and help prevent disease recurrence," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These are the first randomized, controlled, Phase 2 data demonstrating clear efficacy and safety of an oncolytic virus with a checkpoint inhibitor. We are excited to be exploring IMLYGIC with PD-1 and PDL-1 checkpoint inhibitors as well."

The most common adverse events in the IMLYGIC plus YERVOY arm were fatigue (59 percent versus 42 percent, respectively), chills (53 percent versus 3 percent, respectively) and diarrhea (42 percent versus 35 percent, respectively). Evaluation of overall survival (OS) is ongoing and continues to be monitored. IMLYGIC is designed to rupture cancer cells causing the release of tumor-derived antigens, which along with granulocyte-macrophage colony-stimulating factor (GM-CSF), may help to initiate an anti-tumor immune response. However, the exact mechanism of action is unknown. This may be complementary to YERVOY's mechanism of action, as the blockade of cytotoxic T-lymphocyte-associated antigen-4 has been shown to augment activation and proliferation of tumor infiltrating T-effector cells.

In addition, these results follow the presentation of new interim data from a Phase 2 biomarker study, which evaluated CD8+ T cell density in biopsies from patients with unresectable stage IIIB-IVM1c melanoma treated with IMLYGIC. These data were presented at the 13th Congress of the European Association of Dermato Oncology in Athens, Greece. The study demonstrated a significant four-fold mean increase in intratumoral CD8+ cell density in uninjected melanoma lesions among 32 matched biopsy pairs collected at baseline and after two doses of IMLYGIC. The response rate was consistent with other IMLYGIC monotherapy studies and the adverse events profile was consistent with the known safety profile of IMLYGIC.

About the '264 Study

The '264 study is a Phase 1b/2, multicenter, open-label trial evaluating the safety and efficacy of IMLYGIC in combination with YERVOY compared to YERVOY alone in patients with unresectable stage IIIB-IV melanoma. The primary endpoint of the Phase 2 portion of study is ORR. Secondary endpoints include duration of response, disease control rate, PFS, OS and safety. The study randomized 198 patients, 98 in the IMLYGIC plus YERVOY arm and 100 in the YERVOY arm.

About Metastatic Melanoma

Melanoma remains a significant public health concern across the globe. Unlike some other cancers, melanoma incidence rates have doubled in the past 40 years, with 132,000 cases occurring worldwide each year.[1,2] Melanoma is more dangerous than other skin cancers, especially when it spreads to other parts of the body, which is referred to as metastatic disease.[3] The overall five-year risk of relapse after surgery increases as disease stage advances, from 48 percent for stage IIIA to 85 percent for stage IIIC.[4] Risk of recurrence is even higher for patients in stage IV undergoing surgery, with 91 percent experiencing relapse.[5] Despite new options, additional treatments are needed – particularly for patients with metastatic disease.

About IMLYGIC® (talimogene laherparepvec)

IMLYGIC® (talimogene laherparepvec) 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.

IMLYGIC is the first oncolytic viral therapy approved by the U.S. Food and Drug Administration (FDA) based on therapeutic benefit demonstrated in a pivotal study. IMLYGIC is 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 OS or have an effect on visceral metastases.

Important U.S. 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 the 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.
- **Obstructive Airway Disorder:** Obstructive airway disorder has been reported following IMLYGIC® treatment. Use caution when injecting lesions close to major airways.

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 and Medication Guide for IMLYGIC®.

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 malignancies, ranging

from blood cancers to solid tumors. With decades of experience providing therapies for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

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 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. 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 reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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 to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. 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 results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. 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. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. 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. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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 acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. Our stock price is volatile and may be affected by a number of events. 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 our common stock.

The scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

*YERVOY is marketed by Bristol-Myers Squibb

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