Amgen Announces First-In-Human Data Evaluating Investigational Novel BiTE® Immunotherapies AMG 420 And AMG 330 At ASH 2018

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Phase 1 Results of Amgen's BiTE® Platform in Heavily Pre-Treated Patients With Multiple Myeloma and Acute Myeloid Leukemia

FDA Grants Fast Track Designation for AMG 420

THOUSAND OAKS, Calif., Dec. 3, 2018 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the first clinical results from studies evaluating investigational novel bispecific T cell engager (BiTE®) immunotherapies AMG 420 and AMG 330. In two separate Phase 1 dose escalation studies, AMG 420, which targets B-cell maturation antigen (BCMA), and AMG 330, which targets CD33, provided early evidence of tolerability and anti-tumor activity in patients with relapsed and/or refractory multiple myeloma and relapsed or refractory acute myeloid leukemia (AML), respectively. These data were highlighted during oral presentations at the 60th American Society of Hematology (ASH) Annual Meeting & Exposition in San Diego.

BiTE® antibody construct technology, pioneered by Amgen, is an innovative treatment approach that helps the body's immune system attack cancer cells without the removal of immune cells from the patient. Amgen is studying a number of "off-the-shelf" investigational BiTE® immunotherapies, with distinct targets, across a range of hematologic and solid tumors.

"Building on our success with the only approved BiTE® immunotherapy available for patients, Amgen is emphasizing our commitment to the potential of this platform by advancing the development of approximately a dozen novel molecules across hematologic and solid tumor targets in hopes of continuing to offer meaningful advances to patients in need," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "We're encouraged by the early results of investigational BiTE® immunotherapies AMG 420 and AMG 330, especially when considered in the context of these heavily pre-treated patients, many of whom have run out of available options. We look forward to sharing more results from our BiTE® pipeline at future medical meetings."

ASH Abstract #1010: Treatment with AMG 420, an anti-B-Cell Maturation Antigen (BCMA) Bispecific T-cell Engager (BiTE®) Antibody Construct, Induces Minimal Residual Disease (MRD) Negative Complete Responses in Relapsed and/or Refractory (R/R) Multiple Myeloma (MM) Patients: Results of a First-in-Human (FIH) Phase 1 Dose Escalation Study

The data shared at ASH were the first presentation of all endpoints from this Phase 1 dose-escalation trial of AMG 420 in patients with relapsed and/or refractory multiple myeloma. The objectives of the study included assessment of safety, tolerability and anti-tumor activity of AMG 420 per International Myeloma Working Group 2006 Uniform Response Criteria for Multiple Myeloma.

In the study, 42 patients with relapsed and/or refractory multiple myeloma who had progression after at least two prior lines of treatment (including a proteasome inhibitor and an immunomodulatory imide drug) received AMG 420 at varying doses [0.2 to 800 µg/day (d)]. AMG 420 induced clinical responses in 13 patients, including complete responses (CR) in seven patients. Four patients treated at the 400 µg/d dose achieved minimal residual disease (MRD) negative complete responses, meaning that no cancer cells were detectable in the bone marrow. The objective response rate at 400 µg/d was 70 percent (seven of 10 patients), with six patients still responding up to 7.5 months. One dose-limiting toxicity was observed up to the 400 µg/d dose (peripheral polyneuropathy, which improved to baseline after intravenous immunoglobulin and corticosteroid treatment).

Of those patients with serious adverse events (AEs) (n=20, 48 percent), 17 required hospitalization and four had prolonged hospitalization. Serious AEs included infections (n=12), peripheral polyneuropathy (n=2), and one each of liver failure, cardiac failure, edema, biliary obstruction, spinal cord compression, renal failure and weight loss. Treatment-related serious AEs included polyneuropathy (n=2, both grade 3) and edema (n=1, grade 3). Cytokine release syndrome (CRS) was seen in 16 patients (grade 1, n=13; grade 2, n=2; grade 3, n=1). In this study, 800 µg/d was determined to not be tolerable, as two out of the three patients treated at this dose experienced dose-limiting toxicities.

Two patients died during the course of the study from AEs not considered treatment-related. One patient died after the first cycle of treatment from acute respiratory distress due to concurrent flu and aspergillosis. The second patient died from liver failure secondary to a viral infection during the course of treatment.

"These first-in-human data of a BCMA-targeting BiTE® immunotherapy showed encouraging evidence of AMG 420 activity, with no major toxicities up to the 400 µg/d dose in patients with relapsed and/or refractory multiple myeloma who received a median of four prior therapies," said Max S. Topp, M.D., professor, Hospital of Wuerzburg, Germany and AMG 420 clinical study investigator. "Despite recent treatment advances, multiple myeloma continues to be a disease characterized by cycles of relapse and recurrence requiring additional therapies to help control the disease."

Additionally, AMG 420 was granted Fast Track Designation by the U.S. Food and Drug Administration (FDA). Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious conditions.

ASH Abstract #25: A Phase 1 First-in-Human Study of AMG 330, an Anti-CD33 Bispecific T-cell Engager (BiTE®) Antibody Construct, in Relapsed/Refractory Acute Myeloid Leukemia (R/R AML)

In a separate first-in-human Phase 1 dose escalation study, 40 patients with relapsed or refractory AML were enrolled to receive AMG 330 in 12 dose cohorts with a target dose range of 0.5 to 480 µg/d. The study objectives were to evaluate the safety, pharmacokinetics and pharmacodynamics of AMG 330 and to estimate the maximum tolerated dose. Results showed that two patients in the trial achieved a CR at the 240 µg/d dose and two patients achieved a CR with incomplete blood count recovery, one at the 240 µg/d dose and one at the 120 µg/d dose. The CRs were not sustained beyond one cycle of treatment.

Patients in the trial received a median of one (range: 1-6) cycle with AMG 330; the majority of patients discontinued treatment for disease progression. Other reasons for study discontinuation included AEs (n=6, 2 treatment-related) and patient request (n=2).

Serious AEs were seen in 73 percent of patients (treatment-related in 17 patients). The most common serious AEs seen in more than one patient included CRS (n=11), febrile neutropenia (n=7), pneumonia (n=4), leukopenia (n=4), pyrexia (n=3), thrombocytopenia (n=3) and subdural hematoma (n=2). One patient died on study due to AML progression and one due to intracranial hemorrhage (neither treatment-related). There were dose-limiting toxicities of grade 2 CRS and grade 4 ventricular fibrillation with a target dose of 480 µg/d administered as a single-step regimen.

"The majority of adult AML patients will not be cured with standard chemotherapy, underscoring the need for innovative treatment options for those who have relapsed or are refractory to currently available treatments[1]," said Farhad Ravandi, M.D., Janiece and Stephen A. Lasher professor of medicine and chief of section of Developmental Therapeutics in the Department of Leukemia at the University of Texas – MD Anderson Cancer Center and AMG 330 clinical study investigator. "These early data are encouraging as they indicate AMG 330 may have anti-leukemic activity in heavily pretreated patients with relapsed or refractory AML, validating the need for continued evaluation of the BiTE® platform in targeting CD33."

About BiTE® Technology

Bispecific T cell engager (BiTE®) antibody construct is an innovative technology that can be engineered to target any tumor antigen expressed by any type of cancer. The protein molecules are designed to kill malignant cells using the patient's own immune system by bridging T cells to tumor cells. BiTE® antibody construct helps connect the T cells to the targeted cell, with the intent of causing T cells to inject toxins which trigger cancer cell death (apoptosis). Amgen is developing BiTE® antibody constructs to uniquely (or specifically) target numerous hematologic malignancies and solid tumors.

About Amgen's Commitment to Oncology

Amgen 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.

For more information, follow us on www.twitter.com/amgenoncology.

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 current reports on 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, including our devices, 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. 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, including in Puerto Rico, 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. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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.

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References

1. Bose P, Vachhani P, Cortex E. Treatment of Relapsed/Refractory Acute Myeloid Leukemia. *Curr Treat Options Oncol.* 2017;18(3):17.

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