Amgen Presents Data From Pivotal Phase 2 Study Of BLINCYTO™ (blinatumomab) Immunotherapy In Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia

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Secondary Analysis Demonstrates 40 Percent of Patients who Achieved Complete Remission Were Enabled to Proceed to Stem Cell Transplant

THOUSAND OAKS, Calif., Dec. 8, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that new data from a pivotal Phase 2 study evaluating BLINCYTO ™ (blinatumomab) for the treatment of adult patients with relapsed/refractory B-cell precursor acute lymphoblastic leukemia (ALL) was presented at the 56th American Society of Hematology (ASH) Annual Meeting and Exposition.

In one analysis from the '211 study, 40 percent of patients treated with BLINCYTO who achieved a complete remission (CR) or complete remission with partial hematologic recovery (CRh) were enabled to proceed to allogeneic hematopoietic stem cell transplant (HSCT). Additionally, a secondary analysis from the study found that 82 percent of patients who had a CR or CRh also had a minimal residual disease (MRD) response, a measure used to predict disease recurrence in patients with ALL.

"The data from the '211 study expand the evidence of Amgen's BiTE® immunotherapy as an advance in the management of this difficult-to-treat cancer, and importantly, served as the basis for the recent U.S. Food and Drug Administration (FDA) approval of BLINCYTO," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "In this study, BLINCYTO helped patients bridge to a stem cell transplant after achieving a remission, a key goal in the management of ALL, and achieved MRD response in patients, an important parameter in predicting relapse."

In the study, the most frequent grade ≥3 adverse events (AEs) occurring in ≥5 percent of patients were febrile neutropenia (25 percent), neutropenia (16 percent), anemia (14 percent), pneumonia (9 percent), thrombocytopenia (8 percent), hyperglycemia (8 percent), leukopenia (8 percent), alanine aminotransferase increased (7 percent), hypokalemia (7 percent), pyrexia (7 percent), sepsis (6 percent), hypophosphatemia (5 percent). Grade ≥ 3 neurologic events occurred in 13 percent of patients, and grade ≥ 3 cytokine release syndrome occurred in 2 percent of patients.

ASH Abstract 965: Allogeneic Hematopoietic Stem Cell Transplantation Following anti-CD19 BiTE® Blinatumomab in Adult Patients with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia
In one analysis of the '211 study, 40 percent of patients treated with BLINCYTO who achieved a CR or CRh were enabled to proceed to HSCT, including both patients who had received prior HSCT and patients who had not received prior HSCT. Additionally, the analysis found that responses to BLINCYTO were similar between patients who had received prior HSCT and patients who had not received HSCT (45 percent versus 42 percent, respectively).

ASH Abstract 3704: An Evaluation of Molecular Response in a Phase 2 Open-Label, Multicenter Confirmatory Study in Patients With Relapsed/Refractory B-Precursor Acute Lymphoblastic Leukemia Receiving Treatment with the BiTE® antibody construct Blinatumomab
A secondary analysis of the study demonstrated that, among patients receiving BLINCYTO who had a CR or CRh and had evaluable MRD data (n=73), 82 percent had an MRD response, with 70 percent of those patients achieving a complete MRD response. Median overall survival was longer among patients who had a CR or CRh and an MRD response compared to patients who didn't have an MRD response (11.5 months [95 percent CI, 8.5 – not estimable] versus 6.7 months [95 percent CI, 2.0 – not estimable], respectively).

In the U.S., more than 6,000 cases of ALL will be diagnosed in 2014, and in the European Union, it is estimated that more than 7,000 cases of ALL are diagnosed each year.[1,2] In adult patients with relapsed or refractory ALL, median overall survival is just three to five months.[3]

'211 Phase 2 Trial Design
The single arm, open-label, multicenter Phase 2 trial evaluated the safety and efficacy of BLINCYTO in adult patients with Philadelphia chromosome-negative (Ph-) B-precursor ALL who had relapsed or were refractory following treatment with standard front-line chemotherapy or allogeneic stem cell transplant. Patients received up to five four-week cycles of intravenous BLINCYTO treatment. The primary endpoint of the study was the rate of CR/CRh within the first two treatment cycles. Secondary endpoints include duration of CR and CRh, relapse-free survival, overall survival, HSCT realization rate, 100-day mortality rate and adverse events.

About BLINCYTO™ (blinatumomab)
BLINCYTO is the first BiTE® antibody construct and the first single-agent immunotherapy to be approved by the U.S. FDA.[4] BLINCYTO was granted breakthrough therapy and priority review designations by the FDA, and is now approved in the U.S. for the treatment of Ph- relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

About BiTE® Technology
Bispecific T cell engager (BiTE®) antibody constructs are a type of immunotherapy being investigated for fighting cancer by helping the body's immune system to detect and target malignant cells. The modified antibodies are designed to engage two different targets simultaneously, thereby juxtaposing T cells (a type of white blood cell capable of killing other cells perceived as threats) to cancer cells. BiTE® antibody constructs help place the T cells within reach of the targeted cell, with the intent of allowing T cells to inject toxins and trigger the cancer cell to die (apoptosis). BiTE® antibody constructs are currently being investigated for their potential to treat a wide variety of cancers. For more information, visit www.biteantibodies.com.

Important U.S. Product Information
BLINCYTO is indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in

subsequent trials.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO™. Interrupt or discontinue BLINCYTO™ as recommended.**
- **Neurological toxicities, which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO™. Interrupt or discontinue BLINCYTO™ as recommended.**

Contraindications
BLINCYTO™ is contraindicated in patients with a known hypersensitivity to blinatumomab or to any component of the product formulation.

Warnings and Precautions

- Cytokine Release Syndrome (CRS): Life-threatening or fatal CRS occurred in patients receiving BLINCYTO™. Infusion reactions have occurred and may be clinically indistinguishable from manifestations of CRS. Closely monitor patients for signs and symptoms of serious events such as pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased total bilirubin (TBILI), disseminated intravascular coagulation (DIC), capillary leak syndrome (CLS), and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). Interrupt or discontinue BLINCYTO™ as outlined in the Prescribing Information (PI).
- Neurological Toxicities: Approximately 50% of patients receiving BLINCYTO™ in clinical trials experienced neurological toxicities. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 15% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The median time to onset of any neurological toxicity was 7 days. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO™ as outlined in the PI.
- Infections: Approximately 25% of patients receiving BLINCYTO™ experienced serious infections, some of which were life-threatening or fatal. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment. Monitor patients for signs or symptoms of infection and treat appropriately, including interruption or discontinuation of BLINCYTO™ as needed.
- Tumor Lysis Syndrome (TLS): Life-threatening or fatal TLS has been observed. Preventive measures, including pretreatment nontoxic cytoreduction and on treatment hydration, should be used during BLINCYTO™ treatment. Monitor patients for signs and symptoms of TLS and interrupt or discontinue BLINCYTO™ as needed to manage these events.
- Neutropenia and Febrile Neutropenia, including life-threatening cases, have been observed. Monitor appropriate laboratory parameters during BLINCYTO™ infusion and interrupt BLINCYTO™ if prolonged neutropenia occurs
- Effects on Ability to Drive and Use Machines: Due to the possibility of neurological events, including seizures, patients receiving BLINCYTO™ are at risk for loss of consciousness, and should be advised against driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while BLINCYTO™ is being administered.
- Elevated Liver Enzymes: Transient elevations in liver enzymes are associated with BLINCYTO™ treatment. The majority of these events were observed in the setting of CRS. The median time to onset was 15 days. Grade 3 or greater elevations in liver enzymes occurred in 6% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase (GGT), and TBILI prior to the start of and during BLINCYTO™ treatment. BLINCYTO™ treatment should be interrupted if transaminases rise to > 5 times the upper limit o normal (ULN) or if TBILI rises to > 3 times ULN.
- Leukoencephalopathy: Although the clinical significance is unknown, cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO™, especially in patients previously treated with cranial irradiation and anti-leukemic chemotherapy.
- Preparation and administration errors have occurred. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).

Adverse Events
The most commonly reported adverse reactions (≥ 20%) in clinical trials were pyrexia (62%), headache (36%), peripheral edema (25%), febrile neutropenia (25%), nausea (25%), hypokalemia (23%), rash (21%), tremor (20%) and constipation (20%).

Dosage and Administration Guidelines

- BLINCYTO™ is administered as a continuous intravenous infusion at a constant flow rate using an infusion pump which should be programmable, lockable, non-elastomeric, and have an alarm.
- It is very important that the instructions for preparation (including admixing) and administration provided in the full Prescribing Information are strictly followed to minimize medication errors (including underdose and overdose).

Please see full Prescribing Information and medication guide for BLINCYTO at www.BLINCYTO.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 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.

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