BLINCYTO® (Blinatumomab) Improved Overall Survival In Patients With B-Cell Precursor Acute Lymphoblastic Leukemia

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First Immunotherapy to Demonstrate Overall Survival Benefit Compared to Standard of Care in This Difficult-to-Treat Patient Population

Results Presented at EHA Presidential Symposium and Recognized as Top Abstract

THOUSAND OAKS, Calif., June 10, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new data from a prespecified interim analysis of the Phase 3 TOWER study, in which BLINCYTO® (blinatumomab) demonstrated an almost two-fold increase in median overall survival (OS) compared to standard of care (SOC). The randomized, open-label TOWER study evaluated the efficacy of BLINCYTO versus SOC chemotherapy in adult patients with Philadelphia chromosome-negative (Ph-) relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). Results from the analysis showed that median OS was 7.7 months (95 percent CI: 5.6, 9.6) for BLINCYTO versus 4 months (95 percent CI: 2.9, 5.3) for SOC (stratified log-rank test *p*=.012; hazard ratio=0.71). As per the recommendation of an independent data monitoring committee, Amgen ended the study early for efficacy based on these results. The data will be presented during The Presidential Symposium at the 21st Congress of the European Hematology Association (EHA) in Copenhagen.

"Acute lymphoblastic leukaemia is the most aggressive type of B-cell malignancy," said Max S. Topp, M.D., professor and head of haematology, University Hospital of Wuerzburg, Germany. "The data presented today not only reinforce the potential of immunotherapy delivered by T cell engaging bispecific antibody constructs but also validate the efficacy of BLINCYTO in these heavily pretreated patients."

Improvement in OS was consistent across subgroups regardless of age, prior salvage therapy or prior allogeneic stem cell transplant (alloSCT). Serious adverse events included infection, blood and lymphatic system disorders, nervous system disorders and cytokine release syndrome. The BLINCYTO adverse events observed in the TOWER study were consistent with the known safety profile of BLINCYTO.

"This is the first study of an immunotherapy to demonstrate overall survival benefit in adult patients with Ph-negative B-cell precursor relapsed or refractory ALL, a very complex-to-treat disease with limited treatment options," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "BLINCYTO is currently approved for the treatment of Ph-negative B-cell precursor relapsed or refractory ALL under accelerated approval, and we look forward to working with regulatory authorities for a full approval for BLINCYTO in this patient population."

ALL is a rare and rapidly progressing cancer of the blood and bone marrow.[1,2] Adult patients diagnosed with Ph- B-cell precursor ALL are often young, with a median age at diagnosis of 34-39.[3,4] Currently, there is no broadly accepted standard treatment regimen for adult patients with relapsed or refractory ALL beyond chemotherapy.[5] Adults with relapsed or refractory ALL typically have a very poor prognosis, with a median OS of three to five months.[6]

About the TOWER Study

The TOWER study was a Phase 3, randomized, open-label study investigating the efficacy of BLINCYTO versus SOC chemotherapy in adult patients with Ph-relapsed or refractory B-cell precursor ALL. Patients were randomized in a 2:1 ratio to receive BLINCYTO or treatment with investigator choice of one of four protocol defined SOC chemotherapy regimens. The primary endpoint was OS. Secondary endpoints included complete remission and the combined endpoint of complete remission plus complete remission with partial or incomplete hematologic recovery.

The TOWER study is the confirmatory trial for BLINCYTO, and Amgen plans to file for full approval of BLINCYTO based on results from the study. Click here to read about the trial on ClinicalTrials.gov.

About Adult ALL

The incidence of adult ALL in European countries is generally between 0.6 to 0.9 per 100,000 persons per year.[7] In the United States (U.S.), the incidence of adult ALL is approximately 0.9 per 100,000 persons per year.[7] In adult ALL, approximately 75 percent is B-cell precursor ALL, of which 75-80 percent is Ph- and roughly half will be refractory to treatment or experience relapse.[7] Thus, with a population projection of 416 million adults in the European Union (EU),[8] it is estimated that the incidence of adult Ph-relapsed or refractory B-cell precursor ALL in the EU is approximately 900 patients per year.[9] In the U.S., the incidence was approximately 650 patients in 2015.[7]

About BLINCYTO® (blinatumomab)

BLINCYTO is a bispecific CD19-directed CD3 T cell engager (BiTE®) antibody construct that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T cells.

BLINCYTO was granted breakthrough therapy and priority review designations by the U.S. Food and Drug Administration (FDA), and is now approved in the U.S. for the treatment of Ph- relapsed or refractory B-cell precursor ALL. This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials.

In November 2015 BLINCYTO was granted conditional marketing authorization in the EU for the treatment of adults with Ph- relapsed or refractory B-cell precursor 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 EU Product Safety Information

This product is subject to additional monitoring in the EU and EEA. All suspected adverse reactions should be reported in accordance with the national reporting system.

The adverse reactions described in this section were identified in the pivotal clinical study (N=189).The most serious adverse reactions that may occur during blinatumomab treatment include: infections (31.7%), neurologic events (16.4%), neutropenia/febrile neutropenia (15.3%) cytokine release syndrome (0.5%), and tumor lysis syndrome (0.5%). The most common adverse reactions were: infusion-related reactions (67.2%), infections (63.0%), pyrexia (59.8%), headache (34.4%), febrile neutropenia (28%), peripheral edema (25.9%), nausea (24.3%), hypokalaemia (23.8%), constipation (20.6%), anaemia (20.1%), cough (18.5%), diarrhea (18.0%), tremor (17.5%), neutropenia (17.5%), abdominal pain (16.9%), insomnia (15.3%), fatigue (15.3%), and chills (15.3%).

Please refer to the Summary of Product Characteristics for full European prescribing information.

BLINCYTO® U.S. Product Safety Information
Important Safety Information Regarding BLINCYTO® (blinatumomab) U.S. Indication

This safety information is specific to the current U.S. approved indication.

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 have been 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 of 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 with BLINCYTO® treatment. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).

Adverse Reactions

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%), diarrhea (20%) and constipation (20%).

Serious adverse reactions were reported in 65% of patients. The most common serious adverse reactions (≥ 2%) included febrile neutropenia, pyrexia, pneumonia, sepsis, neutropenia, device-related infection, tremor, encephalopathy, infection, overdose, confusion, Staphylococcal bacteremia, and headache.

U.S. 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 U.S. 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 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. 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.

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