FDA APPROVES BLINCYTO® (BLINATUMOMAB) IN CD19-POSITIVE PHILADELPHIA CHROMOSOME-NEGATIVE B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL) IN THE CONSOLIDATION PHASE

June 14, 2024

BLINCYTO® Added to Multiphase Consolidation Chemotherapy Reduced Risk of Death by 58% Showing Superior Overall Survival Versus Chemotherapy Alone

First and Only Bispecific T-cell Engager (BiTE®) Therapy for Consolidation Treatment Regardless of Measurable Residual Disease (MRD) Status

THOUSAND OAKS, Calif., June 14, 2024 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the U.S. Food and Drug Administration (FDA) has approved BLINCYTO® (blinatumomab) for the treatment of adult and pediatric patients one month or older with CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia (B-ALL) in the consolidation phase, regardless of measurable residual disease (MRD) status.

"B-ALL is an aggressive blood cancer with enduring high unmet need. BLINCYTO has helped thousands of patients with B-ALL over the last 10 years. Today's approval in the frontline consolidation phase, regardless of MRD status, allows us to reach more patients than ever with this transformative, first-in-class Bispecific T-cell Engager (BiTE®) therapy," said Jay Bradner, M.D., executive vice president, Research and Development, and chief scientific officer at Amgen.

The approval marks the third indication for BLINCYTO and is based primarily on the Phase 3 E1910 clinical trial led by ECOG-ACRIN Cancer Research Group that studied patients with newly diagnosed Philadelphia chromosome-negative B-ALL receiving postinduction consolidation treatment, which aims to deepen remission to achieve durable responses. Study results demonstrated that BLINCYTO added to multiphase consolidation chemotherapy showed superior overall survival (OS) versus chemotherapy alone. The 3-year OS was 84.8% in the BLINCYTO plus chemotherapy arm (n=112) and 69% in the chemotherapy arm (n=112), with the hazard ratio for OS of 0.42. With a median follow-up of 4.5 years, the 5-year OS was 82.4% in the BLINCYTO plus chemotherapy arm and 62.5% in the chemotherapy arm.

"In the E1910 study, blinatumomab reduced risk of death and showed a remarkable improvement in overall survival," said Selina M. Luger, M.D., professor of hematology-oncology at the University of Pennsylvania's Perelman School of Medicine and Abramson Cancer Center, chair of the ECOG-ACRIN Leukemia Committee and an investigator on the study. "This approval redefines the standard of care for patients with B-ALL and provides them with a more effective treatment option than standard chemotherapy alone."

"The risk of B-ALL recurrence after the initial phase of treatment is relatively high, making this approval for patients noteworthy," said E. Anders Kolb, M.D., president and chief executive officer of The Leukemia & Lymphoma Society. "B-ALL is the most common type of ALL and having another effective option available earlier in a patient's treatment journey is critical for clinicians who are working to give these patients more time with their loved ones."

The E1910 study was designed and conducted independently from industry. ECOG-ACRIN sponsored the trial with public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH). Other NCI-funded network groups took part in the study. In addition, Amgen provided BLINCYTO and support through an NCI Cooperative Research and Development Agreement.

About Acute Lymphoblastic Leukemia (ALL)
ALL, also known as acute lymphoblastic leukemia, is a fast-growing type of blood cancer that develops in the bone marrow and can sometimes spread to other parts of the body, including the lymph nodes, liver, spleen, and central nervous system. ALL is a rare disease, with 6,540 new cases diagnosed in the U.S. in 2023 affecting both children and adults.[1] B-ALL begins in immature cells that would normally develop into B-cell lymphocytes, which are white blood cells that grow in bone marrow.[2,3] B-ALL is the most common type of ALL, constituting approximately 75% of cases in adults.[4]

About BLINCYTO® (blinatumomab)
BLINCYTO is the first globally approved BiTE® immuno-oncology therapy that targets CD19 surface antigens on B cells. BiTE® molecules fight cancer by helping the body's immune system detect and target malignant cells by engaging T cells (a type of white blood cell capable of killing other cells perceived as threats) to cancer cells. By bringing T cells near cancer cells, the T cells can inject toxins and trigger cancer cell death (apoptosis). BiTE® immuno-oncology therapies are currently being investigated for their potential to treat a wide variety of cancers.

BLINCYTO was granted breakthrough therapy and Priority Review designations by the U.S. FDA and is approved in the U.S. for the treatment of:

- Adult and pediatric patients one month or older with CD19-positive Philadelphia chromosome-negative B-ALL during the consolidation phase of multiphase therapy.
- CD19-positive B-ALL in first or second complete remission with MRD greater than or equal to 0.1% in adults and pediatric patients one month or older.
- Relapsed or refractory CD19-positive B-ALL in adults and pediatric patients one month or older.

In the European Union (EU), BLINCYTO is indicated as monotherapy for the treatment of:

- Adults with Philadelphia chromosome-negative CD19-positive relapsed or refractory B-ALL. Patients with Philadelphia chromosome-positive B-ALL should have failed treatment with at least two tyrosine kinase inhibitors (TKIs) and have no

alternative treatment options.
- Adults with Philadelphia chromosome-negative CD19-positive B-ALL in first or second complete remission with MRD greater than or equal to 0.1%.
- Pediatric patients aged 1 year or older with Philadelphia chromosome-negative CD19-positive B-ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.
- Pediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome-negative CD19-positive B-ALL as part of the consolidation therapy.

INDICATIONS

BLINCYTO® (blinatumomab) is indicated for the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients one month and older with:

- Philadelphia chromosome-negative disease in the consolidation phase of multiphase chemotherapy.
- Minimal residual disease (MRD) greater than or equal to 0.1% in first or second complete remission.
- Relapsed or refractory disease.

BLINCYTO® IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® and treat with corticosteroids as recommended.**
- **Neurological toxicities, including immune effector cell-associated neurotoxicity syndrome (ICANS) 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):** CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®. The median time to onset of CRS is 2 days after the start of infusion and the median time to resolution of CRS was 5 days among cases that resolved. Closely monitor and advise patients to contact their healthcare professional for signs and symptoms of serious adverse events such as fever, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased total bilirubin (TBILI), and disseminated intravascular coagulation (DIC). The manifestations of CRS after treatment with BLINCYTO® overlap with those of infusion reactions, capillary leak syndrome (CLS), and hemophagocytic histiocytosis/macrophage activation syndrome (MAS). Using all of these terms to define CRS in clinical trials of BLINCYTO®, CRS was reported in 15% of patients with R/R ALL, in 7% of patients with MRD-positive ALL, and in 16% of patients receiving BLINCYTO® cycles in the consolidation phase of therapy. If severe CRS occurs, interrupt BLINCYTO® until CRS resolves. Discontinue BLINCYTO® permanently if life-threatening CRS occurs. Administer corticosteroids for severe or life-threatening CRS.

- **Neurological Toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome:** BLINCYTO® can cause serious or life-threatening neurologic toxicity, including ICANS. The incidence of neurologic toxicities in clinical trials was approximately 65%. The median time to the first event was within the first 2 weeks of BLINCYTO® treatment. The most common (≥ 10%) manifestations of neurological toxicity were headache and tremor. Grade 3 or higher neurological toxicities occurred in approximately 13% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. Manifestations of neurological toxicity included cranial nerve disorders. The majority of neurologic toxicities resolved following interruption of BLINCYTO®, but some resulted in treatment discontinuation.

  The incidence of signs and symptoms consistent with ICANS in clinical trials was 7.5%. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. There is limited experience with BLINCYTO® in patients with active ALL in the central nervous system (CNS) or a history of neurologic events. Patients with a history or presence of clinically relevant CNS pathology were excluded from clinical studies. Patients with Down Syndrome over the age of 10 years may have a higher risk of seizures with BLINCYTO® therapy.

Monitor patients for signs and symptoms of neurological toxicities, including ICANS, and interrupt or discontinue BLINCYTO® as outlined in the PI. Advise outpatients to contact their healthcare professional if they develop signs or symptoms of neurological toxicities.

- **Infections:** Approximately 25% of patients receiving BLINCYTO® in clinical trials experienced serious infections such as sepsis, pneumonia, bacteremia, opportunistic infections, and catheter-site 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),** which may be life-threatening or fatal, 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 (including, but not limited to, white blood cell count and absolute neutrophil count) 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 and ICANS, 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 with a median time to onset of 3 days. In patients receiving BLINCYTO®, although the majority of these events were observed in the setting of CRS, some cases of elevated liver enzymes were observed outside the setting of CRS, with a median time to onset of 19 days. Grade 3 or greater elevations in liver enzymes occurred in approximately 7% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase, and total blood bilirubin 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 total bilirubin rises to > 3 times ULN.

- **Pancreatitis:** Fatal pancreatitis has been reported in patients receiving BLINCYTO® in combination with dexamethasone in clinical trials and the post-marketing setting. Evaluate patients who develop signs and symptoms of pancreatitis and interrupt or discontinue BLINCYTO® and dexamethasone as needed.

- **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 antileukemic 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).

- **Immunization:** Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to the start of BLINCYTO® treatment, during treatment, and until immune recovery following last cycle of BLINCYTO®.

- **Benzyl Alcohol Toxicity in Neonates:** Serious adverse reactions, including fatal reactions and the "gasping syndrome," have been reported in very low birth weight (VLBW) neonates born weighing less than 1500 g, and early preterm neonates (infants born less than 34 weeks gestational age) who received intravenous drugs containing benzyl alcohol as a preservative. Early preterm VLBW neonates may be more likely to develop these reactions, because they may be less able to metabolize benzyl alcohol.

  Use the preservative-free preparations of BLINCYTO® where possible in neonates. When prescribing BLINCYTO® (with preservative) for neonatal patients, consider the combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative), other products containing benzyl alcohol or other excipients (e.g., ethanol, propylene glycol) which compete with benzyl alcohol for the same metabolic pathway.

  Monitor neonatal patients receiving BLINCYTO® (with preservative) for new or worsening metabolic acidosis. The minimum amount of benzyl alcohol at which serious adverse reactions may occur in neonates is not known. The BLINCYTO® 7-Day

bag (with preservative) contains 7.4 mg of benzyl alcohol per mL.

- **Embryo-Fetal Toxicity:** Based on its mechanism of action, BLINCYTO® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with BLINCYTO® and for 48 hours after the last dose.

Adverse Reactions

- The safety of BLINCYTO® in adult and pediatric patients one month and older with MRD-positive B-cell precursor ALL (n=137), relapsed or refractory B-cell precursor ALL (n=267), and Philadelphia chromosome-negative B cell precursor ALL in consolidation (n=165) was evaluated in clinical studies. The most common adverse reactions (≥ 20%) to BLINCYTO® in this pooled population were pyrexia, infusion-related reactions, headache, infection, musculoskeletal pain, neutropenia, nausea, anemia, thrombocytopenia, and diarrhea.

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 BLINCYTO® full Prescribing Information, including BOXED WARNINGS.

About BiTE® Technology
Bispecific T-cell Engager (BiTE®) technology is a targeted immuno-oncology platform that is designed to engage patient's own T cells to any tumor-specific antigen, activating the cytotoxic potential of T cells to eliminate detectable cancer. The BiTE® immuno-oncology platform has the potential to treat different tumor types through tumor-specific antigens. The BiTE® platform has a goal of leading to off-the-shelf solutions, which have the potential to make innovative T cell treatment available to all providers when their patients need it. Amgen is advancing multiple BiTE® molecules across a broad range of hematologic malignancies and solid tumors, further investigating BiTE® technology with the goal of enhancing patient experience and therapeutic potential. To learn more about BiTE® technology, visit https://www.amgenoncology.com/bite-platform.html.

About Amgen
Amgen discovers, develops, manufactures and delivers innovative medicines to help millions of patients in their fight against some of the world's toughest diseases. More than 40 years ago, Amgen helped to establish the biotechnology industry and remains on the cutting-edge of innovation, using technology and human genetic data to push beyond what's known today. Amgen is advancing a broad and deep pipeline that builds on its existing portfolio of medicines to treat cancer, heart disease, osteoporosis, inflammatory diseases and rare diseases.

In 2024, Amgen was named one of the "World's Most Innovative Companies" by Fast Company and one of "America's Best Large Employers" by Forbes, among other external recognitions. Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average®, and it is also part of the Nasdaq-100 Index®, which includes the largest and most innovative non-financial companies listed on the Nasdaq Stock Market based on market capitalization.

For more information, visit Amgen.com and follow Amgen on X, LinkedIn, Instagram, TikTok, YouTube and Threads.

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 any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd. or Kyowa-Kirin Co., Ltd.), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), the Teneobio, Inc. acquisition, the ChemoCentryx, Inc. acquisition, or the Horizon Therapeutics plc acquisition (including the prospective performance and outlook of Horizon's business, performance and opportunities, any potential strategic benefits, synergies or opportunities expected as a result of such acquisition), and any projected impacts from the Horizon acquisition on our acquisition related expenses going forward, as well as 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, effects of pandemics or other widespread health problems on our business, outcomes, progress, 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. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. 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 collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful. There can be no guarantee that we will be able to realize any of the strategic benefits, synergies or opportunities arising from the Horizon acquisition, and such benefits, synergies or opportunities may take longer to realize than expected. We may not be able to successfully integrate Horizon, and such integration may take longer, be more difficult or cost more than expected. A breakdown, cyberattack or information security breach of our information technology systems 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 and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect our business and operations. Global economic conditions may magnify certain risks that affect our business. 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.

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Editor's note: Dr. Luger has received honoraria for an Amgen-sponsored educational symposium.

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