New Data To Be Presented At ASH 2017 Underscore Amgen's Commitment To Improving Lives And Changing Outcomes For Patients With Difficult-To-Treat Blood Cancers

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Positive Overall Survival Data From Phase 3 ASPIRE Trial on KYPROLIS® (Carfilzomib) in Relapsed Multiple Myeloma to be Highlighted in Oral Presentation

Results From Several Abstracts Highlight the Potential of Amgen's Bispecific T Cell Engager (BiTE®) Platform as an Innovative Approach to Treating Blood Cancers

FDA Grants Priority Review for BLINCYTO (Blinatumomab) Supplemental Biologics License Application in Minimal Residual Disease-Positive Acute Lymphoblastic Leukemia

THOUSAND OAKS, Calif., Dec. 7, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that new clinical data and analyses from 33 abstracts, including six oral presentations, evaluating approved medicines and investigational immuno-oncology agents from the Company's robust hematology portfolio and pipeline will be presented at the 59th American Society of Hematology (ASH) Annual Meeting & Exposition in Atlanta, Dec. 9-12, 2017.

The breadth and depth of data to be presented at ASH highlight Amgen's commitment to advancing treatment options for patients with some of the most difficult-to-treat blood cancers and disorders. Notably at ASH, positive overall survival (OS) results from the Phase 3 ASPIRE trial will be detailed for the first time in an oral presentation, which showed the addition of KYPROLIS® (carfilzomib) to lenalidomide and dexamethasone (KRd) significantly extended OS versus lenalidomide and dexamethasone (Rd) alone in patients with relapsed or refractory multiple myeloma. The safety data from ASPIRE was consistent with the known safety profile of KYPROLIS.

"At Amgen, we take great pride in our heritage and commitment to developing innovative, life-changing treatments for some of the toughest cancers," said David Reese, M.D., senior vice president of Translational Sciences and Oncology at Amgen. "The range of data from our broad portfolio of treatments and innovative pipeline assets together demonstrate the considerable potential of Amgen's investment in oncology and blood cancers. Results being presented at ASH also highlight the potential of BiTEs, our bispecific T cell engager molecules, to activate a patient's immune system to fight cancer, and demonstrate the benefit our approved medicines can provide for patients with blood cancers across the disease continuum."

Translating Research into Improved Survival for Patients

New results to be presented at ASH demonstrate how two Amgen medicines – KYPROLIS and BLINCYTO® (blinatumomab) – improved OS in adult patients with relapsed multiple myeloma and Philadelphia chromosome-negative (Ph-) relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL), respectively.

KYPROLIS-based regimens (KRd) and KYPROLIS® and dexamethasone (Kd) are the first and only to demonstrate improved OS over two standards of care (Rd) and Velcade® (bortezomib) and dexamethasone (Vd) in two Phase 3 trials in relapsed or refractory patients with multiple myeloma. In addition to ASPIRE, OS data from the Phase 3 ENDEAVOR trial will be detailed in presentations, which showed how Kd were superior in improving OS versus Vd across subgroups of relapsed or refractory patients with multiple myeloma.

BLINCYTO is the first-and-only approved CD19-directed CD3 BiTE® immunotherapy and the only treatment to demonstrate a statistically significant improvement inOS in patients with relapsed or refractory ALL. Results from an exploratory analysis evaluating the OS benefit of BLINCYTO maintenance therapy in patients with Ph- relapsed or refractory B-cell precursor ALL will be highlighted during a poster session. BLINCYTO maintenance therapy reduced the risk of death by 41 percent versus no maintenance therapy. Adverse events were consistent with the established safety profile in adult patients with Ph- relapsed or refractory B-cell precursor ALL. Overall safety event rates were lower in maintenance vs. induction or consolidation cycles.

The U.S. Food and Drug Administration (FDA) has accepted for priority review the supplemental Biologics License Application (sBLA) for BLINCYTO for the treatment of patients with frontline or relapsed B-cell precursor ALL with minimal residual disease (MRD), the first application to be submitted for this indication. The Prescription Drug User Fee Act (PDUFA) target action date is March 29, 2018. Results from the Phase 2 BLAST study upon which the sBLA is based were presented at the 57th Annual ASH Meeting and Exposition in 2015.

Advancing Outcomes Across the Disease Continuum

New real-world data in patients with multiple myeloma bone disease will also be presented. Of note, a study evaluating patterns and predictors of initiation of intravenous bisphosphonates among multiple myeloma patients will be highlighted in an oral session. In the study, less than half of patients initiated bisphosphonate treatment in the two years after diagnosis to prevent fractures and other skeletal-related events, underscoring the need to manage the bone health of patients with myeloma more proactively.

Spotlighting Robust Amgen Immuno-Oncology Pipeline

An array of data from the Amgen oncology pipeline will be presented at ASH, spanning a variety of modalities across immuno-oncology. Notably, four presentations will focus on the potential of Amgen's BiTE® platform as a novel immuno-oncology approach to treating a variety of hematologic cancers. Amgen is the only company with an approved BiTE® (BLINCYTO) and believes that this technology platform holds significant potential in other hematologic cancers and in solid tumors.

Amgen Investor Webcast

Amgen will host a webcast investor meeting at ASH on Saturday, Dec. 9, 2017, at 11:30 a.m. ET. David M. Reese, M.D., senior vice president of Translational Sciences and Oncology at Amgen, together with other members of Amgen's management team and a clinical investigator, will participate to discuss the Company's oncology program, including Amgen's BiTE® immunotherapy platform.

Live audio of the investor meeting will be broadcast over the internet simultaneously and will be available to members of the news media, investors and the general public.

The webcast, as with other selected presentations regarding developments in Amgen's business given at certain investor and medical conferences, can be accessed on Amgen's website, www.amgen.com, under Investors. Information regarding presentation times, webcast availability and webcast links are noted on Amgen's Investor Relations Events Calendar. The webcast will be archived and available for replay for at least 90 days after the event.

Key Amgen presentation information for ASH 2017 is featured here. A complete listing of abstracts can be found on the ASH website.

Translating Research into Improved Survival for Patients

- **Overall Survival (OS) of Patients With Relapsed/Refractory Multiple Myeloma (RRMM) Treated With Carfilzomib, Lenalidomide, and Dexamethasone (KRd) Versus Lenalidomide and Dexamethasone (Rd): Final Analysis From the Randomized Phase 3 ASPIRE Trial**
  Abstract #743, Oral Presentation, Monday, Dec. 11 at 2:45 p.m. ET in Georgia World Congress Center, Building C, Level 1, Hall C1
- **Overall Survival of Relapsed/Refractory Multiple Myeloma Patients Treated With Carfilzomib and Dexamethasone vs Bortezomib and Dexamethasone: Results From the Phase 3 ENDEAVOR Study According to Age Subgroup**
  Abstract #1885, Poster Presentation, Saturday, Dec. 9 at 5:30 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2
- **Overall Survival of Patients With Relapsed Multiple Myeloma Treated With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone According to Prior Line of Therapy and Previous Exposure to Bortezomib: Secondary Analysis of the Phase 3 ENDEAVOR Study**
  Abstract #1850, Poster Presentation, Saturday, Dec. 9 at 5:30 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2
- **Maintenance Therapy With Blinatumomab in Adults With Relapsed/Refractory B-Precursor Acute Lymphoblastic Leukemia (ALL): Overall Survival in Adults Enrolled In a Phase 3 Open-Label Trial**
  Abstract #2552, Poster Presentation, Sunday, Dec. 10 at 6 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2

Advancing Outcomes Across the Disease Continuum

- **Patterns and Predictors of Initiation of Intravenous Bisphosphonates Among Patients With Multiple Myeloma in the United States**
  Abstract #534, Oral Presentation, Sunday, Dec. 10 at 4:30 p.m. ET in Georgia World Congress Center, Building B, Level 2, B206
- **Multiple Myeloma Patients and Risk of SRE – Real-World Evidence in US Oncology Clinics**
  Abstract #2171, Poster Presentation, Saturday, Dec. 9 at 5:30 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2

Spotlighting Robust Amgen Immuno-Oncology Pipeline

- **Preclinical Characterization of AMG 424, a Novel Humanized T Cell–Recruiting Bispecific Anti-CD3/CD38 Antibody**
  Abstract #500, Oral Presentation, Sunday, Dec. 10 at 4:30 p.m. ET in Georgia World Congress Center, Building B, Level 3, B308-B309
- **CD33/CD3-Bispecific T-Cell Engaging (BiTE®) Antibody Constructs Efficiently Target Monocytic CD14+HLA-DRlow IDO+AML-MDSCs**
  Abstract #1363, Poster Presentation, Saturday, Dec. 9 at 5:30 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2
- **Evaluation of a FLT3 BiTE® for Acute Myeloid Leukemia**
  Abstract #1354, Poster Presentation, Saturday, Dec. 9 at 5:30 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2
- **Generation of a Half-life Extended Anti-CD19 BiTE® Antibody Construct Compatible With Once-weekly Dosing for Treatment of CD19-positive Malignancies**
  Abstract #2815, Poster Presentation, Sunday, Dec. 10 at 6 p.m. ET in Georgia World Congress Center, Building A, Level 1, Hall A2
- **AMG 592 is an Investigational IL-2 Mutein That Induces Highly Selective Expansion of Regulatory T cells**
  Abstract #696, Oral Presentation, Monday, Dec. 11 at 2:45 p.m. ET in Georgia World Congress Center, Building C, Level 1, C108-C109

About KYPROLIS® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[1] KYPROLIS has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[1] In some cells, KYPROLIS can cause cell death,

especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[1,2]

KYPROLIS is approved in the U.S. for the following:

- In combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- As a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

KYPROLIS is also approved in Argentina, Australia, Bahrain, Canada, Hong Kong, Israel, Japan, Kuwait, Lebanon, Macao, Mexico, Thailand, Colombia, S. Korea, Qatar, Switzerland, United Arab Emirates, Turkey, Russia, Brazil, India, Oman and the European Union. Additional regulatory applications for KYPROLIS are underway and have been submitted to health authorities worldwide.

IMPORTANT SAFETY INFORMATION

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of KYPROLIS. Some events occurred in patients with normal baseline ventricular function. Death due to cardiac arrest has occurred within one day of KYPROLIS administration.
- Monitor patients for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart KYPROLIS at 1 dose level reduction based on a benefit/risk assessment.
- While adequate hydration is required prior to each dose in Cycle 1, monitor all patients for evidence of volume overload, especially patients at risk for cardiac failure. Adjust total fluid intake as clinically appropriate in patients with baseline cardiac failure or who are at risk for cardiac failure.
- Patients ≥ 75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, conduction abnormalities, angina, or arrhythmias may be at greater risk for cardiac complications and should have a comprehensive medical assessment (including blood pressure and fluid management) prior to starting treatment with KYPROLIS and remain under close follow-up.

Acute Renal Failure

- Cases of acute renal failure and renal insufficiency adverse events (including renal failure) have occurred in patients receiving KYPROLIS. Acute renal failure was reported more frequently in patients with advanced relapsed and refractory multiple myeloma who received KYPROLIS monotherapy. Monitor renal function with regular measurement of the serum creatinine and/or estimated creatinine clearance. Reduce or withhold dose as appropriate.

Tumor Lysis Syndrome

- Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred in patients receiving KYPROLIS. Patients with multiple myeloma and a high tumor burden should be considered at greater risk for TLS. Adequate hydration is required prior to each dose in Cycle 1, and in subsequent cycles as needed. Consider uric acid lowering drugs in patients at risk for TLS. Monitor for evidence of TLS during treatment and manage promptly. Withhold KYPROLIS until TLS is resolved.

Pulmonary Toxicity

- Acute Respiratory Distress Syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have occurred in patients receiving KYPROLIS. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported in patients treated with KYPROLIS. Evaluate with cardiac imaging and/or other tests as indicated. Withhold KYPROLIS for PAH until resolved or returned to baseline and consider whether to restart KYPROLIS based on a benefit/risk assessment.

Dyspnea

- Dyspnea was reported in patients treated with KYPROLIS. Evaluate dyspnea to exclude cardiopulmonary conditions including cardiac failure and pulmonary syndromes. Stop KYPROLIS for Grade 3 or 4 dyspnea until resolved or returned to baseline. Consider whether to restart KYPROLIS based on a benefit/risk assessment.

Hypertension

- Hypertension, including hypertensive crisis and hypertensive emergency, has been observed with KYPROLIS. Some of these events have been fatal. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold KYPROLIS and evaluate. Consider whether to restart KYPROLIS based on a benefit/risk assessment.

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed with KYPROLIS. Thromboprophylaxis is recommended for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- Patients using oral contraceptives or a hormonal method of contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment with KYPROLIS in combination with dexamethasone or lenalidomide plus dexamethasone.

Infusion Reactions

- Infusion reactions, including life-threatening reactions, have occurred in patients receiving KYPROLIS.
- Symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration of KYPROLIS. Premedicate with dexamethasone to reduce the incidence and severity of infusion reactions. Inform patients of the risk and of symptoms of an infusion reaction and to contact a physician immediately if they occur.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported in patients receiving KYPROLIS. Hemorrhagic events have included gastrointestinal, pulmonary, and intracranial hemorrhage and epistaxis. Promptly evaluate signs and symptoms of blood loss. Reduce or withhold dose as appropriate.

Thrombocytopenia

- KYPROLIS causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Thrombocytopenia was reported in patients receiving KYPROLIS. Monitor platelet counts frequently during treatment with KYPROLIS. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have been reported during treatment with KYPROLIS. KYPROLIS can cause increased serum transaminases. Monitor liver enzymes regularly regardless of baseline values. Reduce or withhold dose as appropriate.

Thrombotic Microangiopathy

- Cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), including fatal outcome have occurred in patients receiving KYPROLIS. Monitor for signs and symptoms of TTP/HUS. Discontinue KYPROLIS if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS therapy in patients previously experiencing TTP/HUS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. PRES was formerly known as Reversible Posterior Leukoencephalopathy Syndrome. Consider a neuro-radiological imaging (MRI) for onset of visual or neurological symptoms. Discontinue KYPROLIS if PRES is suspected and evaluate. The safety of reinitiating KYPROLIS therapy in patients previously experiencing PRES is not known.

Increased Fatal and Serious Toxicities in Combination with Melphalan and Prednisone in Newly Diagnosed Transplant-ineligible Patients

- In a clinical trial of transplant-ineligible patients with newly diagnosed multiple myeloma comparing KYPROLIS, melphalan, and prednisone (KMP) vs bortezomib, melphalan, and prednisone (VMP), a higher incidence of serious and fatal adverse events was observed in patients in the KMP arm. KYPROLIS in combination with melphalan and prednisone is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma.

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals.

- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

ADVERSE REACTIONS

- The most common adverse reactions occurring in at least 20% of patients treated with KYPROLIS in the combination therapy trials: anemia, neutropenia, diarrhea, dyspnea, fatigue, thrombocytopenia, pyrexia, insomnia, muscle spasm, cough, upper respiratory tract infection, hypokalemia.
- The most common adverse reactions occurring in at least 20% of patients treated with KYPROLIS in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please see full prescribing information at www.kyprolis.com.

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 FDA, and is now approved in the U.S. for the treatment of relapsed or refractory B-cell precursor ALL in adults and children.

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. Additional regulatory applications for BLINCYTO are underway and have been submitted to health authorities worldwide.

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 bridge T cells to tumor cells, using the patient's own immune system to eradicate their cancer. 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.

BLINCYTO® U.S. Product Safety Information

Indication and Important Safety Information, including Boxed WARNINGS, for BLINCYTO® (blinatumomab) for injection, for intravenous use

INDICATION

BLINCYTO® is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

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): CRS, which may be life-threatening or fatal, 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 65% of patients receiving BLINCYTO® in clinical trials experienced neurological toxicities. The median time to the first event was within the first 2 weeks of BLINCYTO® treatment and the majority of events resolved. The most common (≥ 10%) manifestations of neurological toxicity were headache and tremor. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 13% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. 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): 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 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 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 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 (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.
- 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®.
- Risk of Serious Adverse Reactions in Pediatric Patients due to Benzyl Alcohol Preservative: Serious and fatal adverse reactions including "gasping syndrome," which is characterized by central nervous system depression, metabolic acidosis, and gasping respirations, can occur in neonates and infants treated with benzyl alcohol-preserved drugs including BLINCYTO® (with preservative). When prescribing BLINCYTO® (with preservative) for pediatric patients, consider combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative) and other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known. Due to the addition of bacteriostatic saline, 7-day bags of BLINCYTO® solution for infusion with preservative contain benzyl alcohol and are not recommended for use in any patients weighing < 22 kg.

Adverse Reactions

- The most common adverse reactions in Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL (TOWER Study) (≥ 20%) in the BLINCYTO® arm were infections (bacterial and pathogen unspecified), pyrexia, headache, infusion-related reactions, anemia, febrile neutropenia, thrombocytopenia, and neutropenia. Serious adverse reactions were reported in 62% of patients. The most common serious adverse reactions (≥ 2%) included febrile neutropenia, pyrexia, sepsis, pneumonia, overdose, septic shock, CRS, bacterial sepsis, device related infection, and bacteremia.
- Adverse reactions that were observed more frequently (≥ 10%) in the pediatric population compared to the adult population were pyrexia (80% vs. 61%), hypertension (26% vs. 8%), anemia (41% vs. 24%), infusion-related reaction (49% vs. 34%), thrombocytopenia (34% vs. 21%), leukopenia (24% vs. 11%), and weight increased (17% vs. 6%).
- In pediatric patients less than 2 years old (infants), the incidence of neurologic toxicities was not significantly different than for the other age groups, but its manifestations were different; the only event terms reported were agitation, headache, insomnia, somnolence, and irritability. Infants also had an increased incidence of hypokalemia (50%) compared to other pediatric age cohorts (15-20%) or adults (17%).

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, including Boxed WARNINGS and Medication Guide, for BLINCYTO®.

About XGEVA® (denosumab)
XGEVA targets the RANKL pathway to prevent the formation, function and survival of osteoclasts, which break down bone. As a monoclonal antibody, XGEVA is not cleared by the kidneys. XGEVA is indicated for the prevention of skeletal-related events in patients with bone metastases from solid tumors. In the U.S., XGEVA currently has a limitation of use noting that it is not indicated for the prevention of skeletal-related events in patients with multiple myeloma. XGEVA is also indicated for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. XGEVA is also indicated in the U.S. for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

U.S. Important Safety Information

Hypocalcemia
Pre-existing hypocalcemia must be corrected prior to initiating therapy with XGEVA®. XGEVA® can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Monitor calcium levels, especially in the first weeks of initiating therapy, and administer calcium, magnesium, and vitamin D as necessary. Monitor levels more frequently when XGEVA® is administered with other drugs that can also lower calcium levels. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.

An increased risk of hypocalcemia has been observed in clinical trials of patients with increasing renal dysfunction, most commonly with severe dysfunction (creatinine clearance less than 30 mL/minute and/or on dialysis), and with inadequate/no calcium supplementation. Monitor calcium levels and calcium and vitamin D intake.

Hypersensitivity
XGEVA® is contraindicated in patients with known clinically significant hypersensitivity to XGEVA®, including anaphylaxis that has been reported with use of XGEVA®. Reactions may include hypotension, dyspnea, upper airway edema, lip swelling, rash, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue XGEVA® therapy permanently.

Drug Products with Same Active Ingredient
Patients receiving XGEVA® should not take Prolia® (denosumab).

Osteonecrosis of the Jaw
Osteonecrosis of the jaw (ONJ) has been reported in patients receiving XGEVA®, manifesting as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration, or gingival erosion. Persistent pain or slow healing of the mouth or jaw after dental surgery may also be manifestations of ONJ. In clinical trials in patients with osseous metastasis, the incidence of ONJ was higher with longer duration of exposure.

Patients with a history of tooth extraction, poor oral hygiene, or use of a dental appliance are at a greater risk to develop ONJ. Other risk factors for the development of ONJ include immunosuppressive therapy, treatment with angiogenesis inhibitors, systemic corticosteroids, diabetes, and gingival infections.

Perform an oral examination and appropriate preventive dentistry prior to the initiation of XGEVA® and periodically during XGEVA® therapy. Advise patients regarding oral hygiene practices. Avoid invasive dental procedures during treatment with XGEVA®. Consider temporarily interrupting XGEVA® therapy if an invasive dental procedure must be performed.

Patients who are suspected of having or who develop ONJ while on XGEVA® should receive care by a dentist or an oral surgeon. In these patients, extensive dental surgery to treat ONJ may exacerbate the condition.

Atypical Subtrochanteric and Diaphyseal Femoral Fracture
Atypical femoral fracture has been reported with XGEVA®. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution.

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. During XGEVA® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patients presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of XGEVA® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Hypercalcemia Following Treatment Discontinuation in Patients with Growing Skeletons
Clinically significant hypercalcemia has been reported in XGEVA® treated patients with growing skeletons, weeks to months following treatment discontinuation. Monitor patients for signs and symptoms of hypercalcemia and treat appropriately.

Embryo-Fetal Toxicity
XGEVA® can cause fetal harm when administered to a pregnant woman. Based on findings in animals, XGEVA® is expected to result in adverse reproductive effects.

Advise females of reproductive potential to use highly effective contraception during therapy, and for at least 5 months after the last dose of XGEVA®. Apprise the patient of the potential hazard to a fetus if XGEVA® is used during pregnancy or if the patient becomes pregnant while patients are

exposed to XGEVA®.

Adverse Reactions
The most common adverse reactions in patients receiving XGEVA® with bone metastasis from solid tumors were fatigue/asthenia, hypophosphatemia, and nausea. The most common serious adverse reaction was dyspnea. The most common adverse reactions resulting in discontinuation were osteonecrosis and hypocalcemia.

The most common adverse reactions in patients receiving XGEVA® for giant cell tumor of bone were arthralgia, headache, nausea, back pain, fatigue, and pain in extremity. The most common serious adverse reactions were osteonecrosis of the jaw and osteomyelitis. The most common adverse reactions resulting in discontinuation of XGEVA® were osteonecrosis of the jaw and tooth abscess or tooth infection.

The most common adverse reactions in patients receiving XGEVA® for hypercalcemia of malignancy were nausea, dyspnea, decreased appetite, headache, peripheral edema, vomiting, anemia, constipation, and diarrhea.

Denosumab is also marketed as Prolia® in other indications.

Please visit www.amgen.com or www.xgeva.com for Full U.S. Prescribing Information.

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 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. Further, 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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