Amgen Announces Data Being Presented At ASH 2019

December 2, 2019

Results From Phase 3 CANDOR Study Evaluating KYPROLIS® (Carfilzomib) in Combination With DARZALEX® (Daratumumab) in Relapsed or Refractory Multiple Myeloma Patients Accepted as Late-Breaking Abstract

New Data From the Children's Oncology Group Phase 3 Trial (AALL1331) of BLINCYTO® (Blinatumomab) Versus Chemotherapy in First Relapse of Acute Lymphoblastic Leukemia Accepted as Late-Breaking Abstract

Data From Amgen's BiTE® Platform Demonstrate Versatility of Approach Across Four Hematological Malignancies

THOUSAND OAKS, Calif., Dec. 2, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new clinical data from its oncology in-line products and pipeline that will be presented at the 61st American Society of Hematology (ASH) Annual Meeting & Exposition in Orlando, Dec. 7-10, 2019.

The Phase 3 CANDOR study, which was accepted as a late-breaking abstract, evaluated KYPROLIS® (carfilzomib) in combination with dexamethasone and DARZALEX® (daratumumab) (KdD) compared to KYPROLIS and dexamethasone alone (Kd) in patients with relapsed or refractory multiple myeloma. Additional data from Amgen's hematology franchise will include new results from the bispecific T cell engager (BiTE®) platform across multiple blood cancers, including multiple myeloma, acute myeloid leukemia, acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma and non-Hodgkin's lymphoma.

"The late-breaking abstract from the CANDOR study evaluating KYPROLIS with an anti-CD38 monoclonal antibody demonstrates that by combining these two powerful agents, this regimen has the potential to be practice-changing for the treatment of patients with relapsed or refractory multiple myeloma," said David M. Reese, M.D., executive vice president of Research and Development at Amgen.

Additionally, data from study AALL1331 conducted by the Children's Oncology Group (COG) evaluating BLINCYTO® (blinatumomab) versus chemotherapy in first relapse of childhood B-lymphoblastic leukemia (B-ALL) were accepted as a late-breaking abstract. AALL1331 is sponsored by the Cancer Therapy Evaluation Program of the National Cancer Institute (NCI), part of the National Institutes of Health, and is conducted by the NCI-funded COG. Amgen provided BLINCYTO for the study under a Collaborative Research and Development Agreement between the NCI and Amgen. BLINCYTO, which was approved in 2014, is the first and only approved BiTE molecule.

"The data being presented at ASH demonstrate our commitment to furthering the science of our in-line products, including KYPROLIS and BLINCYTO, while also advancing our pipeline of innovative BiTE molecules which could potentially provide new treatment approaches for patients across blood cancers for which there remains high unmet need," continued Reese.

A complete listing of Amgen's abstracts is available on the ASH website. Notable abstracts include:

KYPROLIS Amgen Sponsored Abstracts

- **Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study CANDOR (NCT03158688)**
  LBA-6, Tuesday, Dec. 10 from 7:30 – 9 a.m. ET in Hall D, Level 2
- **Efficacy And Safety Of Carfilzomib-Lenalidomide-Dexamethasone (KRd) In NDMM: Pooled Analysis Of 4 Single-Arm Studies**
  Abstract #1891, Poster Presentation, Poster I, Saturday, Dec. 7 from 5:30 – 7:30 p.m. ET in Hall B, Level 2
- **Phase 1b Study Of Carfilzomib In Combination With Induction Chemotherapy In Children With Relapsed Or Refractory Acute Lymphoblastic Leukemia (ALL)**
  Abstract #3873, Poster Presentation, Poster III, Monday, Dec. 9 from 6 – 8 p.m. ET in Hall B, Level 2

KYPROLIS Investigator Led Abstracts

- **Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd) Induction, Autologous Transplantation and Post-Transplant, Response-Adapted, Measurable Residual Disease (MRD)-Based Dara-KRd Consolidation in Patients with Newly Diagnosed Multiple Myeloma (NDMM)**
  Abstract #860, Oral Presentation, Monday, Dec. 9 at 4:45 p.m. in Hall E2
- **Weekly Carfilzomib, Lenalidomide, Dexamethasone And Daratumumab (wKRd-D) Combination Therapy Provides Unprecedented MRD Negativity Rates In Newly Diagnosed Multiple Myeloma: A Clinical And Correlative Phase 2 Study**
  Abstract #862, Oral Presentation, Monday, Dec. 9 at 5:15 p.m. in Hall E2, Level 2

BLINCYTO Amgen Sponsored Abstracts

- **Blinatumomab in Pediatric Patients With R/R B-Cell Precursor And Molecularly Resistant ALL: Updated Analysis of 110 Patients Treated in an Expanded Access Study (RIALTO)**
  Abstract #1294, Poster Presentation, Poster I, Saturday, Dec. 7 from 5:30 – 7:30 p.m. ET in Hall B, Level 2

- **Open-Label, Phase 2 Study of Blinatumomab After First-Line Rituximab-Chemotherapy in Adults with Newly Diagnosed, High-Risk Diffuse Large B-Cell Lymphoma**
  Abstract #4077, Poster Presentation, Poster III, Monday, Dec. 9 from 6 – 8 p.m. ET in Hall B, Level 2
- **Treatment of Adults with Relapsed/Refractory Philadelphia Chromosome Negative Acute Lymphoblastic Leukemia with Blinatumomab in a Real-World Setting: Results from the Neuf Study**
  Abstract #2627, Poster Presentation, Poster II, Sunday, Dec. 8 from 6 – 8 p.m. ET in Hall B, Level 2
- **Treatment of Adults with Minimal Residual Disease (MRD) Positive Acute Lymphoblastic Leukemia with Blinatumomab in a Real-World Setting: Results from the Neuf Study**
  Abstract #2624, Poster Presentation, Poster II, Sunday, Dec. 8 from 6 – 8 p.m. ET in Hall B, Level 2

BLINCYTO Investigator Led Abstracts

- **A Randomized Phase 3 Trial of Blinatumomab vs Chemotherapy as Post-Reinduction Therapy in High & Intermediate Risk First Relapse of B-ALL in Children & AYAs Demonstrates Superior Survival and Tolerability of Blin: A Report from Children's Oncology Group Study AALL1331**
  LBA-1, Late-Breaking Oral Presentation, Tuesday, Dec. 10 from 7:30 – 9 a.m. ET in Hall D, Level 2
- **A Phase IB Study of Blinatumomab (blina) in Patients with B Cell Acute Lymphoblastic Leukemia (ALL) and B-Cell Non-Hodgkin Lymphoma (NHL) As Post-Allogeneic Blood or Marrow Transplant (allo-BMT) Remission Maintenance**
  Abstract #778, Oral Presentation, Monday, Dec. 9 at 3:30 p.m. in Chapin Theater (W320), Level 3
- **Blinatumomab/Lenalidomide in Relapsed/Refractory Non-Hodgkin's Lymphoma: A Phase I California Cancer Consortium Study of Safety, Efficacy and Immune Correlative Analysis**
  Abstract #760, Oral Presentation, Monday, Dec. 9 at 3:30 p.m. in W304ABCD, Level 3
- **Updated Results of A Phase II Study of Reduced-Intensity Chemotherapy With Mini-Hyper-CVD In Combination With Inotuzumab Ozogamicin, With or Without Blinatumomab, in Older Adults with Newly Diagnosed Philadelphia Chromosome-Negative Acute Lymphoblastic Leukemia**
  Abstract #823, Oral Presentation, Monday, Dec. 9 at 4:30 p.m. in Tangerine 1 (WF1), Level 2

XGEVA® (denosumab)

- **Progression Free Survival Analysis Of Denosumab Vs Zoledronic Acid In Intent To Transplant Multiple Myeloma Patients Based On Treatment Regimen And Baseline Characteristics**
  Abstract #606, Oral Presentation, Monday, Dec. 9 at 8:15 a.m. in Sunburst Room (W340)

Oncology Pipeline

- **AMG 701 Potently Induces Anti-Multiple Myeloma (MM) Functions Of T Cells And IMiDs Further Enhance Its Efficacy To Prevent MM Relapse In Vivo**
  Abstract #135, Oral Presentation, Saturday, Dec. 7 at 10 a.m. ET in Valencia A (W415A), Level 4
- **Preliminary Results From A Phase 1 First-in-Human Study Of AMG 673, A Novel Half-life Extended (HLE) Anti-CD33/CD3 BiTE® (Bispecific T-cell Engager) Molecule In Patients With Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML)**
  Abstract #833, Oral Presentation, Monday, Dec. 9 at 5:30 p.m. ET in Chapin Theater (W320), Level 3

About CANDOR
CANDOR, a randomized, open-label Phase 3 study of KYPROLIS, dexamethasone and DARZALEX (KdD) compared to KYPROLIS and dexamethasone (Kd), has evaluated 466 relapsed or refractory multiple myeloma patients who have received one to three prior therapies. Patients were treated until disease progression. The primary endpoint was PFS, and the key secondary endpoints were overall response rate, minimal residual disease and overall survival. PFS was defined as time from randomization until disease progression or death from any cause.

In the first arm, patients received KYPROLIS twice weekly at 56 mg/m^2 and dexamethasone in combination with DARZALEX. In the second arm (control), patients received KYPROLIS twice weekly at 56 mg/m^2 and dexamethasone.

CANDOR was initiated as part of a collaboration with Janssen, and under the terms of the agreement, Janssen co-funded the study. For more information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT03158688.

About the COG AALL1331 Study
The COG AALL1331 study is a risk-stratified, randomized, Phase 3 trial of blinatumomab in first relapse of pediatric B-ALL to evaluate disease-free survival (DFS) of high-risk (HR) and intermediate-risk (IR) relapsed B-ALL patients who are randomized following induction block 1 chemotherapy to receive either two intensive chemotherapy blocks or two 5-week blocks of blinatumomab. It also compares the DFS of low risk (LR) relapse B-ALL patients who are randomized following block 1 chemotherapy to receive either chemotherapy alone or chemotherapy plus blinatumomab. Key secondary endpoints include overall survival of HR, IR, and LR relapsed B-ALL patients. This is a global study that is being conducted in Australia, Canada, New Zealand and United States. Click here to read about the trial on ClinicalTrials.gov.

About Multiple Myeloma
Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[1] It is a rare and life-threatening disease that accounts for approximately one percent of all cancers.[2,3] Worldwide, approximately 160,000 people are diagnosed with multiple myeloma each

year, and 106,000 patient deaths are reported on an annual basis.[2]

About KYPROLIS® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[4] KYPROLIS has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[5] 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.[4,5]

Since its first approval in 2012, more than 125,000 patients worldwide have received KYPROLIS. 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 Algeria, Argentina, Australia, Bahrain, Belarus, Brazil, Canada, Chile, Colombia, Ecuador, Egypt, European Union, Hong Kong, India, Israel, Japan, Jordan, Kuwait, Lebanon, Macao, Malaysia, Mexico, Morocco, New Zealand, Oman, Philippines, Qatar, Russia, Saudi Arabia, Singapore, S. Korea, Switzerland, Taiwan, Thailand, Turkey and United Arab Emirates.

Important U.S. KYPROLIS® (carfilzomib) 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 administration.
- Monitor patients for signs or symptoms of cardiac failure or 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 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.
- For 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 prior to starting treatment with KYPROLIS and remain under close follow-up with fluid management.

Acute Renal Failure

- Cases of acute renal failure, including some fatal renal failure events, and renal insufficiency adverse events (including renal failure) have occurred. 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. Patients with 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, and withhold until 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. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported. 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 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 based on a benefit/risk assessment.

Hypertension

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

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed. 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 hormonal contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment.

Infusion Reactions

- Infusion reactions, including life-threatening reactions, have occurred. 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. Premedicate with dexamethasone to reduce the incidence and severity of infusion reactions. Inform patients of the risk and of symptoms and seek immediate medical attention if they occur.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported. 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. Monitor platelet counts frequently during treatment. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have occurred. 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. Monitor for signs and symptoms of TTP/HUS. Discontinue if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. If PRES is suspected, discontinue and evaluate with appropriate imaging. The safety of reinitiating KYPROLIS 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. KMP 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.
- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS and for 3 months following the final dose. 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 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 in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral

Please see full Prescribing Information at www.kyprolis.com.

About ALL and MRD

ALL is a rapidly progressing cancer of the blood and bone marrow that occurs in both adults and children.[6,7] Poor outcomes have been observed in patients who achieve first or second complete hematologic remission but are persistently MRD-positive, which currently remains detectable at the molecular level after treatment.[8,9] For more information about MRD, please visit AmgenOncology.com.

About BiTE® Technology

Bispecific T cell engager (BiTE®) technology is a targeted immuno-oncology platform that is designed to engage patients' 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 leads 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 more than a dozen 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.

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.

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.

BLINCYTO was granted breakthrough therapy and priority review designations by the U.S. Food and Drug Administration and is approved in the U.S. for the treatment of:

- relapsed or refractory B-cell precursor ALL in adults and children.
- B-cell precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children.
  This indication is approved under accelerated approval based on MRD response rate and hematological relapse-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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-precursor acute lymphoblastic leukaemia (ALL).
- adults with Philadelphia chromosome negative CD19 positive B-precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%.
- paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor 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

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® and treat with corticosteroids 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 15% of patients with R/R ALL

and in 7% of patients with MRD-positive ALL. 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, and hemophagocytic histiocytosis/macrophage activation syndrome. 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: 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. Manifestations of neurological toxicity included cranial nerve disorders. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO® as outlined in the PI.
- 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, 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 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 the 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 (≥ 20%) in clinical trial experience of patients with MRD-positive B-cell precursor ALL (BLAST Study) treated with BLINCYTO® were pyrexia (91%), infusion-related reactions (77%), headache (39%), infections (pathogen unspecified 39%), tremor (31%), and chills (28%). Serious adverse reactions were reported in 61% of patients. The most common serious adverse reactions (≥ 2%) included pyrexia, tremor, encephalopathy, aphasia, lymphopenia, neutropenia, overdose, device related infection, seizure, and staphylococcal infection.
- The most common adverse reactions (≥ 20%) in clinical trial experience of patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL (TOWER Study) treated with BLINCYTO® 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 adults with relapsed or refractory B-cell precursor ALL 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 and medication guide for BLINCYTO at www.BLINCYTO.com.

About Multiple Myeloma and Bone Complications

Multiple myeloma is the second most common hematologic cancer, and it develops in plasma cells located in the bone marrow microenvironment.[2,10] It is typically characterized by osteolytic bone lesions as well as renal failure, which are both part of diagnosis (CRAB criteria).[11] Each year an estimated 160,000 new cases of multiple myeloma are diagnosed worldwide, resulting in more than 106,000 deaths per year.[2]

More than 90 percent of patients develop osteolytic lesions during the course of the disease.[12] Preventing bone complications is a critical aspect of caring for patients with multiple myeloma, because these events can result in significant morbidity.[13] Current treatment options to prevent bone complications are limited to bisphosphonates, including zoledronic acid, which are cleared through the kidneys.[14] Approximately 60 percent of all multiple myeloma patients have or will develop renal impairment over the course of the disease.[15]

About XGEVA® (denosumab)

XGEVA targets the RANKL pathway to prevent the formation, function and survival of osteoclasts, which break down bone. XGEVA is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. XGEVA is also indicated for 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 and for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

INDICATIONS

XGEVA® is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. XGEVA® is indicated for 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 indicated for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

IMPORTANT SAFETY INFORMATION
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 cancer, 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 Giant Cell Tumor of Bone (GCTB) and in Patients with Growing Skeletons
Clinically significant hypercalcemia requiring hospitalization and complicated by acute renal injury has been reported in XGEVA®-treated patients with GCTB and in patients with growing skeletons within one year of treatment discontinuation. Monitor patients for signs and symptoms of hypercalcemia after treatment discontinuation and treat appropriately.

Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation
Multiple vertebral fractures (MVF) have been reported following discontinuation of treatment with denosumab. Patients at higher risk for MVF include those with risk factors for or a history of osteoporosis or prior fractures. When XGEVA® treatment is discontinued, evaluate the individual patient's risk for vertebral fractures.

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 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.

For multiple myeloma patients receiving XGEVA®, the most common adverse reactions were diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache. The most common serious adverse reaction was pneumonia. The most common adverse reaction resulting in discontinuation of XGEVA® was osteonecrosis of the jaw.

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.

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

About Amgen Oncology

Amgen Oncology is searching for and finding answers to incredibly complex questions that will advance care and improve lives for cancer patients and their families. Our research drives us to understand the disease in the context of the patient's life – not just their cancer journey – so they can take control of their lives.

For the last four decades, we have been dedicated to discovering the firsts that matter in oncology and to finding ways to reduce the burden of cancer. Building on our heritage, Amgen continues to advance the largest pipeline in the Company's history, moving with great speed to advance those innovations for the patients who need them.

At Amgen, we are driven by our commitment to transform the lives of cancer patients and keep them at the center of everything we do.

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

About Amgen
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaboration with any other company, including BeiGene, Ltd., or the acquisition of Otezla® (apremilast), including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion, 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 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. 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 or products, and to integrate the operations of companies or in support of products we have acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the

product candidates. Further, any 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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