Amgen Announces New Data Being Presented At ASH 2021

December 6, 2021

BLINCYTO® (blinatumomab) Data Demonstrate Superior Overall Survival in Pediatric Patients With Relapsed Acute Lymphoblastic Leukemia in Longer Follow-up of Phase 3 Trial

First Presentation of Efficacy and Safety Data With Subcutaneous BLINCYTO Administration in Patients With Relapsed or Refractory Acute Lymphoblastic Leukemia

THOUSAND OAKS, Calif., Dec. 6, 2021 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced new data from its hematology pipeline and marketed portfolio to be presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition in Atlanta, Georgia, and virtually, from Dec. 11-14, 2021.

"The data being presented at ASH demonstrates Amgen's commitment to reaching more patients with our innovative hematology medicines and improving the patient experience by exploring more convenient administrations for people living with blood cancers," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "By accelerating the development and delivery of transformative medicines in difficult to treat and vulnerable patient populations, including children and pregnant women, we continue to focus on the relentless pursuit of breakthroughs for blood cancer patients and their families."

Amgen will present data on its bispecific T-cell engager (BiTE®) platform, including BLINCYTO® (blinatumomab), as well as KYPROLIS® (carfilzomib) and Nplate® (romiplostim). Updated data from the Phase 3 '215 trial in children with high-risk first relapse B-cell precursor acute lymphoblastic leukemia (B-ALL) showed BLINCYTO improved event-free survival (EFS) and overall survival (OS) versus chemotherapy before allogeneic hematopoietic stem cell transplant (alloHSCT). The first presentation of safety and efficacy data with BLINCYTO administered subcutaneously in adults with relapsed or refractory B-ALL also demonstrated encouraging results.

Additionally, results from the Phase 1b study investigating KYPROLIS in combination with vincristine, dexamethasone, PEG-asparaginase, daunorubicin (VXLD) induction therapy in children with relapsed or refractory ALL showing promising efficacy in highly advanced relapsed/refractory pediatric ALL will be presented in a poster discussion session. Analyses from the Pregnancy Surveillance Program (PSP) evaluating pregnancy and fetal outcomes of women exposed to Nplate highlighting no substantial safety concerns identified for mothers, fetuses and infants due to Nplate use during pregnancy will also be shared as an oral presentation on Monday, Dec. 13, 2021.

Abstracts are available on the ASH website.

Key Abstracts and Presentation Times:

Disease State Amgen Sponsored Abstracts

- **Real World Assessment of Treatment Patterns and Outcomes Among Multiple Myeloma Patients Across Different Risk Stratification Criteria in the United States: A Retrospective Cohort Study**
  Abstract #1640, Poster Presentation, Saturday, Dec. 11 from 5:30 – 7:30 p.m. ET
- **Outcomes of Triple-Class (Proteasome Inhibitor, Immunomodulator, CD38 Monoclonal Antibody) Exposed Relapsed or Refractory Multiple Myeloma (RRMM) in United States (US) Real-World Practice**
  Abstract #3042, Poster Presentation, Sunday, Dec. 12 from 6 – 8 p.m. ET
- **A Temporal and Multinational Assessment of Acute Myeloid Leukemia (AML) Cancer Incidence, Survival and Disease Burden**
  Abstract #4124, Poster Presentation, Monday, Dec. 13 from 6 – 8 p.m. ET

BLINCYTO Amgen Sponsored Abstracts

- **Superior Overall Survival With Blinatumomab Versus Chemotherapy in Children With High-Risk First Relapse of B-cell Precursor Acute Lymphoblastic Leukemia: A Randomized, Controlled Phase 3 Trial**
  Abstract #1231, Poster Presentation, Saturday, Dec. 11 from 5:30 – 7:30 p.m. ET
- **Safety and Efficacy of Subcutaneous (SC) Blinatumomab for the Treatment of Adults with Relapsed or Refractory B Cell Precursor Acute Lymphoblastic Leukemia (R/R B-ALL)**
  Abstract #2303, Poster Presentation, Sunday, Dec. 12 from 6 – 8 p.m. ET
- **A Phase 1b Study of Blinatumomab Regimen Including Subcutaneous Administration in Relapsed / Refractory (R/R) Indolent Non-Hodgkin's Lymphoma (NHL)**
  Abstract #2436, Poster Presentation, Sunday, Dec. 12 from 6 – 8 p.m. ET
- **Heterogeneity of Minimal/Measurable Residual Disease (MRD) Practices in Adult B-Cell Precursor Acute Lymphoblastic Leukemia (BCP-ALL) in the United States**
  Online Publication

BLINCYTO Investigator Sponsored Studies (ISS)

- **Updated Results From a Phase II Study of Hyper-CVAD with Sequential Blinatumomab in Adults with Newly Diagnosed Philadelphia Chromosome-Negative B-cell Acute Lymphoblastic Leukemia**
  Abstract #1233, Poster Presentation, Saturday, Dec. 11 from 5:30 – 7:30 p.m. ET
- **A Randomized Phase 3 Trial of Blinatumomab vs. Chemotherapy as Post-Reinduction Therapy in Low Risk (LR) First Relapse of B-Acute Lymphoblastic Leukemia (B-ALL) in Children and Adolescents/Young Adults (AYAs): A Report from Children's Oncology Group Study**
  Abstract #363, Oral Presentation, Sunday, Dec. 12 at 10 a.m. ET

KYPROLIS Amgen Sponsored Abstracts

- **Phase 1b Study of Carfilzomib in Combination with Induction Chemotherapy in Children with Relapsed or Refractory Acute Lymphoblastic Leukemia (ALL)**
  Abstract #1235, Poster Presentation, Saturday, Dec. 11 from 5:30 – 7:30 p.m. ET
- **Phase 2 Study of Carfilzomib in Combination with Induction Chemotherapy in Children with Relapsed or Refractory Acute Lymphoblastic Leukemia (ALL)**
  Abstract #4403, Online Publication

KYPROLIS Investigator Sponsored Studies (ISS)

- **Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd), Autologous Transplantation and MRD Response-Adapted Consolidation and Treatment Cessation. Final Primary Endpoint Analysis of the MASTER Trial**
  Abstract #481, Oral Presentation, Sunday, Dec. 12 at 12 p.m. ET
- **Biologic Basis of the Impact of Autologous Hematopoietic Cell Transplantation in Multiple Myeloma Treated with Quadruplet Therapy**
  Abstract #483, Oral Presentation, Sunday, Dec. 12 at 12:30 p.m. ET

Nplate Clinical Data Abstracts

- **Surveillance Program of Romiplostim Use Connected to Pregnancy**
  Abstract #585, Oral Presentation, Monday, Dec. 13 from 10:30 a.m. – 12 p.m. ET
- **Romiplostim for the Treatment of Adult Patients with Newly Diagnosed or Persistent Immune Thrombocytopenia: Subgroup Analysis from a Phase 2 Study**
  Abstract #3157, Poster Presentation, Monday, Dec. 13 from 6 – 8 p.m. ET
- **Thrombocytopenia Among Patients with Hematologic Malignancies and Solid Tumors: Risk and Prognosis**
  Abstract #3156, Poster Presentation, Monday, Dec. 13 from 6 – 8 p.m. ET
- **Investigating the Potential Impact of Dosing Tolerance to Facilitate Use of Nplate Self-Administration in Adult Patients with ITP**
  Online Publication
- **Assessing Romiplostim Dose and Platelet Response-Guided Titration to Support Use of Romiplostim in ITP Patients Less Than 12 months From Diagnosis**
  Online Publication

Nplate Investigator Sponsored Studies (ISS)

- **Immunomodulation with Romiplostim in Young Adult Primary Immune Thrombocytopenia (ITP) As Second-Line Strategy (iROM-study)**
  Abstract #3149, Poster Presentation, Monday, Dec. 13 from 6 – 8 p.m. ET

About the 20120215 Study

Study 20120215 is a Phase 3 open-label, multicenter, randomized, controlled trial evaluating event-free survival (EFS) after treatment with BLINCYTO compared with standard of care consolidation chemotherapy in pediatric patients with high-risk first-relapse B-cell ALL. In September 2019, the BLINCYTO arm showed superior efficacy on the primary endpoint of EFS, exceeding the prespecified stopping boundary; based on the recommendation from the Independent Data Monitoring Committee (DMC), Amgen terminated enrollment. Key secondary endpoints included overall survival and MRD response, adverse events (AEs), 100-day mortality after alloHSCT, incidence of anti-blinatumomab antibody formation, cumulative incidence of relapse. This is a global study that is being conducted as part of the PIP (Pediatric Investigation Plan) agreed to between Amgen and the EMA and is being conducted in Australia and various countries in the EU and Latin America. Click here to read about the trial on ClinicalTrials.gov.

About BLINCYTO® (Blinatumomab)

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

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

- relapsed or refractory CD-19 positive B-cell precursor ALL in adults and children.
- CD-19 positive 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 leukemia (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%.
- pediatric 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 BiTE® Technology

BiTE® (bispecific T cell engager) technology is a targeted immuno-oncology platform that is designed to engage patient's own T cells to any tumor-specific antigen, activating the cytotoxic potential of T cells to eliminate detectable cancer. The BiTE immuno-oncology platform has the potential to treat different tumor types through tumor-specific antigens. The BiTE platform has a goal of leading to off-the-shelf solutions, which have the potential to make innovative T cell treatment available to all providers when their patients need it. Amgen is advancing 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. To learn more about BiTE technology, visit www.AmgenBiTETechnology.com.

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.[2] 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]

Since its first approval in 2012, approximately 200,000 patients worldwide have received KYPROLIS.[3] KYPROLIS is approved in the U.S. for the following:

- for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with
  - Lenalidomide and dexamethasone; or
  - Dexamethasone; or
  - Daratumumab and dexamethasone.
- 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, Kazakhstan, Kuwait, Lebanon, Macao, Malaysia, Mexico, Morocco, New Zealand, Oman, Peru, Philippines, Qatar, Russia, Saudi Arabia, Serbia, Singapore, S. Africa, S. Korea, Switzerland, Taiwan, Thailand, Turkey and United Arab Emirates.

U.S. KYPROLIS® (carfilzomib) Important Safety Information

INDICATIONS

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- KYPROLIS® is indicated as a single agent for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), 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 reactions 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 of age, 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 (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. Provide thromboprophylaxis for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- For patients using hormonal contraception associated with a risk of thrombosis, consider an alternative method of effective contraception during treatment.

Infusion Reactions

- Infusion reactions, including life–threatening reactions, have occurred. Signs and symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, laryngeal 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.

Progressive Multifocal Leukoencephalopathy (PML)

- Cases of PML, including fatal cases, have occurred. In addition to KYPROLIS, other contributary factors may include prior or concurrent use of immunosuppressive therapy. Consider PML in any patient with new onset of or changes in pre-existing neurological signs or symptoms. If PML is suspected, discontinue and initiate evaluation for PML including neurology consultation.

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 reactions 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.
- Advise pregnant women of the potential risk to a fetus. Females of reproductive potential should use effective contraception during treatment with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should use effective contraception during treatment with KYPROLIS and for 3 months following the final dose.

Adverse Reactions

- The most common adverse reactions in the combination therapy trials: anemia, diarrhea, fatigue, hypertension, pyrexia, upper respiratory tract infection, thrombocytopenia, cough, dyspnea, and insomnia.
- The most common adverse reactions in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please see accompanying full Prescribing Information.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[4] It is a rare and life-threatening disease that accounts for approximately one percent of all cancers.[4,5] Worldwide, approximately 176,000 people are diagnosed with multiple myeloma each year, and 117,000 patient deaths are reported on an annual basis.[5]

About Nplate® (romiplostim)

Nplate is a thrombopoietin (TPO) receptor agonist that mimics the body's natural TPO and is designed to increase platelet counts in patients with ITP.[6]

In the U.S:

- Nplate is approved for the treatment of thrombocytopenia in adult patients with ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
- Nplate is approved for the treatment of thrombocytopenia in pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

In the European Union (EU):

- Nplate is indicated for the treatment of primary ITP in adult patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).
- Nplate is indicated for the treatment of chronic primary ITP in pediatric patients one year of age and older who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).

Nplate is also approved in 69 countries, including Canada and Australia.

For more information about Nplate, please visit www.Nplate.com.

IMPORTANT SAFETY INFORMATION

Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia

- In Nplate® (romiplostim) clinical trials of patients with myelodysplastic syndromes (MDS) and severe thrombocytopenia, progression from MDS to acute myelogenous leukemia (AML) has been observed.
- Nplate® is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than

ITP.

Thrombotic/Thromboembolic Complications

- Thrombotic/thromboembolic complications may result from increases in platelet counts with Nplate® use. Portal vein thrombosis has been reported in patients with chronic liver disease receiving Nplate®.
- To minimize the risk for thrombotic/thromboembolic complications, do not use Nplate® in an attempt to normalize platelet counts. Follow the dose adjustment guidelines to achieve and maintain a platelet count of ≥ 50 x 10^9/L.

Loss of Response to Nplate®

- Hyporesponsiveness or failure to maintain a platelet response with Nplate® should prompt a search for causative factors, including neutralizing antibodies to Nplate®.
- To detect antibody formation, submit blood samples to Amgen (1–800–772–6436). Amgen will assay these samples for antibodies to Nplate® and thrombopoietin (TPO).
- Discontinue Nplate® if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the highest weekly dose of 10 mcg/kg.

Adverse Reactions

Adult ITP

- In the placebo-controlled trials of adult ITP patients, headache was the most commonly reported adverse drug reaction, occurring in 35% of patients receiving Nplate® and 32% of patients receiving placebo. Adverse drug reactions in adults with a ≥ 5% higher patient incidence in Nplate® versus placebo were Arthralgia (26%, 20%), Dizziness (17%, 0%), Insomnia (16%, 7%), Myalgia (14%, 2%), Pain in Extremity (13%, 5%), Abdominal Pain (11%, 0%), Shoulder Pain (8%, 0%), Dyspepsia (7%, 0%), and Paresthesia (6%, 0%).
- The safety profile of Nplate was similar across patients, regardless of ITP duration. The following adverse reactions (at least 5% incidence and at least 5% more frequent with Nplate compared with placebo or standard of care) occurred in Nplate patients with ITP duration up to 12 months: bronchitis, sinusitis, vomiting, arthralgia, myalgia, headache, dizziness, diarrhea, upper respiratory tract infection, cough, nausea and oropharyngeal pain. The adverse reaction of thrombocytosis occurred with an incidence of 2% in adults with ITP duration up to 12 months.

Pediatric ITP

- The most common adverse reactions experienced by ≥ 5% of patients receiving Nplate with ≥ 5% higher incidence in the romiplostim arm across the two placebo-controlled trials were contusion (41%), upper respiratory tract infection (31%), oropharyngeal pain (25%), pyrexia (24%), diarrhea (20%), rash (15%), and upper abdominal pain (14%).
- In pediatric patients of age ≥ 1 year receiving romiplostim for ITP, adverse reactions with an incidence of ≥ 25% in the two randomized trials were: contusion (41%), upper respiratory tract infection (31%), and oropharyngeal pain (25%).

Nplate® administration may increase the risk for development or progression of reticulin fiber formation within the bone marrow. This formation may improve upon discontinuation of Nplate®. In a clinical trial, one patient with ITP and hemolytic anemia developed marrow fibrosis with collagen during Nplate® therapy.

INDICATIONS

Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate® is indicated for the treatment of thrombocytopenia in pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Nplate® is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP. Nplate® should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. Nplate® should not be used in an attempt to normalize platelet counts.

Please see full Prescribing Information and Medication Guide.

About Amgen Oncology

At Amgen Oncology, our mission to serve patients drives all that we do. That's why we're relentlessly focused on accelerating the delivery of medicines that have the potential to empower all angles of care and transform lives of people with cancer.

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're advancing oncology at the speed of life™.

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.

Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average and is also part of the Nasdaq-100 index. In 2021, Amgen was named one of the 25 World's Best Workplaces™ by *Fortune* and Great Place to Work™ and one of the 100 most sustainable companies in the world by *Barron's*.

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

Forward-Looking Statement
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd., Kyowa-Kirin Co., Ltd., or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), the Five Prime Therapeutics, Inc. acquisition, or the Teneobio, Inc. acquisition, as well as estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes, effects of pandemics or other widespread health problems such as the ongoing COVID-19 pandemic on our business, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful. 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. Global economic conditions may magnify certain risks that affect our business. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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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References

1. Moreau P, et al. *Blood*. 2012;120(5):947-59.
2. Kortuem KM and Stewart AK. *Blood*. 2013; 7;121(6):893
3. Amgen Data on File.
4. Jakubowiak A. *Semin Hematol*. 2012; 49 Suppl 1: S16-S32.
5. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021; 71(3):209-249.
6. Nplate® (romiplostim) prescribing information, Amgen.