Amgen Highlights Data To Be Presented At 21st Congress Of The European Hematology Association

May 19, 2016

BLINCYTO® (Blinatumomab) TOWER Study Demonstrates Improved Overall Survival Versus Standard of Care in Patients With B-Cell Precursor Acute Lymphoblastic Leukemia

TOWER Study to be Presented at Presidential Symposium as a Best Abstract

Sub-group Analyses From Pivotal Head-To-Head Phase 3 Studies Provide Further Insight Into Kyprolis® (Carfilzomib) as Treatment Option for Patients With Multiple Myeloma

Aranesp® (Darbepoetin Alfa) Phase 3 ARCADE Data Demonstrates Significant Reduction in Red Blood Cell Transfusions in Anemic Patients With Myelodysplastic Syndrome

THOUSAND OAKS, Calif., May 19, 2016 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced it will present new data from its oncology portfolio at the 21st Congress of the European Hematology Association (EHA), June 9-12, 2016, in Copenhagen. Key data to be presented include studies evaluating BLINCYTO® (blinatumomab), Kyprolis® (carfilzomib), Aranesp® (darbepoetin alfa) and Nplate® (romiplostim). Data from the BLINCYTO TOWER study will be presented during the Presidential Symposium on Friday, June 10, and is recognized as a top abstract submitted to the Congress. This, along with other presentations, reinforces Amgen's commitment to serve patients with hematologic malignancies through the development of innovative and novel products.

"We are excited that the data from the TOWER study, which is the first randomized study of an immunotherapy to demonstrate overall survival benefit in adult patients with Ph-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia, will be featured at the Presidential Symposium this year at EHA," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "This recognition along with other key data being presented validates our ongoing commitment to developing innovative therapies that have the potential to tackle unmet needs in complex-to-treat patient populations."

Key data include findings from clinical trials in acute lymphoblastic leukemia (ALL), multiple myeloma (MM), myelodysplastic syndrome (MDS) and immune thrombocytopenia (ITP):

BLINCYTO data

BLINCYTO was granted conditional marketing authorization by the European Commission (EC) last November and is the first bispecific T cell engager (BiTE®) antibody construct approved in the European Union (EU) for the treatment of adults with Philadelphia chromosome-negative (Ph-) relapsed or refractory B-cell precursor ALL. Data from the comprehensive ALL development program to be presented will include:

- **Blinatumomab Improved Overall Survival in Patients with Relapsed/Refractory Philadelphia Negative B-Cell Precursor Acute Lymphoblastic Leukemia in a Randomized, Open-Label Phase 3 Study (TOWER)**
  Abstract No. S149, Oral presentation, Presidential symposium, Friday, June 10, 2016, 4:45 – 5 p.m. (CEST), Hall A1

ALL data

- **Trends in the Use of Hematopoietic Stem Cell Transplantation for Adults with Acute Lymphoblastic Leukemia (ALL): A Report From the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation (EBMT)**
  Abstract No. S524, Oral presentation, Stem cell transplantation - Clinical 1, Saturday, June 11, 2016, 4:45 – 5 p.m. (CEST), Room H5

Kyprolis data

Kyprolis was granted marketing authorization by the EC last November for use in combination treatment of patients with relapsed multiple myeloma. Data to be presented include:

- **Carfilzomib, Lenalidomide, and Dexamethasone vs. Lenalidomide and Dexamethasone in Patients with Relapsed Multiple Myeloma: Analysis of Response and Progression-Free Survival Hazard Ratio Over Time**
  Abstract No. P275, Poster presentation, Innovative therapies for MM 1, Friday, June 10, 2016 , 5:15 – 6:45 p.m. (CEST), Poster area (Hall H)
- **Outcomes for Asian Patients with Relapsed Multiple Myeloma Treated with Carfilzomib and Dexamethasone vs. Bortezomib and Dexamethasone: A Subgroup Analysis of the Phase 3 ENDEAVOR Study (NCT01568866)**
  Abstract No. E1328, Eposter presentation, Myeloma and other monoclonal gammopathies – Clinical
- **Carfilzomib and Dexamethasone vs. Subcutaneous Bortezomib and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma: Secondary Analysis from the Phase 3 Study ENDEAVOR (NCT01568866)**
  Abstract No. P659, Poster presentation, Innovative therapies for MM 4 Saturday, June 11, 2016, 5:30 – 7 p.m. (CEST), Poster area (Hall H)
- **Efficacy and Safety by Cytogenetic Risk Status: Phase 3 Study (ASPIRE) of Carfilzomib, Lenalidomide and Dexamethasone Versus Lenalidomide and Dexamethasone in Patients with Relapsed Multiple Myeloma**

Abstract No. P663, Poster presentation, Innovative therapies for MM 4, Saturday, June 11, 2016, 5:30 – 7 p.m. (CEST), Poster area (Hall H)

- **A Sub-Study of the Phase 3 ENDEAVOR Study: Serial Echocardiographic Assessment of Patients with Relapsed Multiple Myeloma (RMM) Receiving Carfilzomib Plus Dexamethasone or Bortezomib Plus Dexamethasone**
  Abstract No. P664, Poster presentation, Innovative therapies for MM 4, Saturday, June 11, 2016, 5:30 – 7 p.m. (CEST), Poster area (Hall H)
- **Carfilzomib and Dexamethasone vs. Bortezomib and Dexamethasone: Subgroup Analysis of Patients with Relapsed Multiple Myeloma by Baseline Cytogenetic Risk Status (Phase 3 ENDEAVOR Study)**
  Abstract No. E1267, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Carfilzomib and Dexamethasone vs. Bortezomib and Dexamethasone in Patients with Relapsed Multiple Myeloma: Analysis of the Phase 3 ENDEAVOR Study by Age Subgroup**
  Abstract No. E1274, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Carfilzomib and Dexamethasone vs. Bortezomib and Dexamethasone: Subgroup Analysis of the Phase 3 ENDEAVOR Study to Evaluate the Impact of Prior Treatment on Patients with Relapsed Multiple Myeloma**
  Abstract No. E1266, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Weekly Carfilzomib with Dexamethasone for Patients with Relapsed or Refractory Multiple Myeloma: Updated Results from the Phase 1/2 Study CHAMPION-1 (NCT01677858)**
  Abstract No. P661, Poster presentation, Innovative therapies for MM 4, Saturday, June 11, 2016, 5:30 – 7 p.m. (CEST), Poster area (Hall H)
- **The Effect of Level of Response to Treatment on Associated Costs and Healthcare Resource Utilization: A Retrospective Chart Review Study in Patients with Symptomatic Multiple Myeloma**
  Abstract No. E1310, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Survival and Treatment Patterns in Patients with Symptomatic Multiple Myeloma (MM) in A Real-World Setting**
  Abstract No. E1280, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Description of Patient Characteristics, Treatment Patterns and Resource Use for Patients with Multiple Myeloma Treated in Three Local Health Units (LHUS) in Italy**
  Abstract No. E1327, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical
- **Overall Survival in Patients with Symptomatic Multiple Myeloma in the Real-World Setting: A Retrospective Analysis of the Pharos Registry in the Netherlands**
  Abstract No. E1292, Eposter presentation, Myeloma and other monoclonal gammopathies - Clinical

Aranesp data

Aranesp received initial EU approval within oncology in August 2002 and is indicated for the treatment of symptomatic anemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy. Data to be presented include:

- **ARCADE (20090160): A Phase 3 Randomized Placebo-Controlled Double-Blind Trial of Darbepoetin Alfa in the Treatment Of Anemia in Patients with Low or Intermediate-1 Risk Myelodysplastic Syndromes (MDS)**
  Abstract No.S128, Oral presentation, Myelodysplastic syndromes – Clinical, Friday, June 10, 2016, 11:30 – 11:45 a.m. (CEST), Hall C14

Nplate data

Nplate, a thrombopoietin receptor agonist, was approved in the EU in February 2009 for the treatment of adult chronic-immune (idiopathic)-thrombocytopenic-purpura (ITP) patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). Data to be presented include:

- **Romiplostim in Splenectomized (Splnx) and Nonsplenectomized (Nonsplnx) Patients with Immune Thrombocytopenia (ITP)**
  Abstract No. S520, Oral presentation, Platelet disorders 1, Saturday, June 11, 2016, 5 – 5:15 p.m. (CEST), Room H4
- **Characterization of Patients with Immune Thrombocytopenia (ITP) Entering Remission in a Romiplostim Bone Marrow Study**
  Abstract No. P405, Poster presentation, Platelet disorders, Friday, June 10, 2016, 5:15 – 6:45 p.m. (CEST), Poster area (Hall H)
- **Safety and Efficacy of Long-Term Open-Label Dosing of Subcutaneous (SC) Romiplostim in Children with Immune Thrombocytopenia (ITP)**
  Abstract No. E1416, Eposter presentation, Platelet disorders
- **Primary Immune Thrombocytopenia Treated with Romiplostim in Routine Clinical Practice: A Retrospective Study from the United Kingdom Immune Thrombocytopenia Registry**
  Abstract No. E1426, Eposter presentation, Platelets disorders
- **Romiplostim in Children with Immune Thrombocytopenia: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study**
  Abstract No. P401, Poster presentation, Platelet disorders, Friday, June 10, 2016, 5:15 – 6:45 p.m. (CEST), Poster area

(Hall H)

- **Safety and Efficacy/Effectiveness of Second-Line Treatments in Patients with Immune Thrombocytopenia: A Systematic Review of the Literature**
  Abstract No. E1417, Eposter presentation, Platelets disorders

Abstracts are available and can be viewed on the EHA website at http://learningcenter.ehaweb.org/eha/#!*menu=16*browseby=2*sortby=1*media=3*label=9759.

About BLINCYTO® (blinatumomab)

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

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

In November 2015, BLINCYTO was granted conditional marketing authorization in the European Union for the treatment of adults with Ph- relapsed or refractory B-cell precursor ALL.

Important EU BLINCYTO® (blinatumomab) Safety Information

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

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

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

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

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

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® as recommended.**
- **Neurological toxicities, which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® as recommended.**

Contraindications

BLINCYTO® is contraindicated in patients with a known hypersensitivity to blinatumomab or to any component of the product formulation.

Warnings and Precautions

Cytokine Release Syndrome (CRS): Life-threatening or fatal CRS occurred in patients receiving BLINCYTO®. Infusion reactions have occurred and may be clinically indistinguishable from manifestations of CRS. Closely monitor patients for signs and symptoms of serious events such as pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased total bilirubin (TBILI), disseminated intravascular coagulation (DIC), capillary leak syndrome (CLS), and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). Interrupt or discontinue BLINCYTO® as outlined in the Prescribing Information (PI).

Neurological Toxicities: Approximately 50% of patients receiving BLINCYTO® in clinical trials experienced neurological toxicities. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 15% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The median time to onset of any neurological toxicity was 7 days. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO® as outlined in the PI.

Infections: Approximately 25% of patients receiving BLINCYTO® experienced serious infections, some of which were life-threatening or fatal. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment. Monitor patients for signs or symptoms of infection and treat appropriately, including interruption or discontinuation of BLINCYTO® as needed.

Tumor Lysis Syndrome (TLS): Life-threatening or fatal TLS has been observed. Preventive measures, including pretreatment nontoxic cytoreduction and on treatment hydration, should be used during BLINCYTO® treatment. Monitor patients for signs and symptoms of TLS and interrupt or discontinue BLINCYTO® as needed to manage these events.

Neutropenia and Febrile Neutropenia, including life-threatening cases, have been observed. Monitor appropriate laboratory parameters during BLINCYTO® infusion and interrupt BLINCYTO® if prolonged neutropenia occurs.

Effects on Ability to Drive and Use Machines: Due to the possibility of neurological events, including seizures, patients receiving BLINCYTO® are at risk for loss of consciousness, and should be advised against driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while BLINCYTO® is being administered.

Elevated Liver Enzymes: Transient elevations in liver enzymes have been associated with BLINCYTO® treatment. The majority of these events were observed in the setting of CRS. The median time to onset was 15 days. Grade 3 or greater elevations in liver enzymes occurred in 6% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase (GGT), and TBILI prior to the start of and during BLINCYTO® treatment. BLINCYTO® treatment should be interrupted if transaminases rise to > 5 times the upper limit of normal (ULN) or if TBILI rises to > 3 times ULN.

Leukoencephalopathy: Although the clinical significance is unknown, cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO® especially in patients previously treated with cranial irradiation and anti-leukemic chemotherapy. Preparation and administration errors have occurred with BLINCYTO® treatment. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).

Adverse Reactions

The most commonly reported adverse reactions (≥ 20%) in clinical trials were pyrexia (62%), headache (36%), peripheral edema (25%), febrile neutropenia (25%), nausea (25%), hypokalemia (23%), rash (21%), tremor (20%), diarrhea (20%) and constipation (20%).

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

U.S. Dosage and Administration Guidelines

BLINCYTO® is administered as a continuous intravenous infusion at a constant flow rate using an infusion pump which should be programmable, lockable, non-elastomeric, and have an alarm. It is very important that the instructions for preparation (including admixing) and administration provided in the full Prescribing Information are strictly followed to minimize medication errors (including underdose and overdose).

Please see full U.S. Prescribing Information and medication guide for BLINCYTO® at www.BLINCYTO.com.

About 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.[2] The irreversibility of Kyprolis' binding has also been shown to offer a more sustained inhibition of the targeted enzymes.[3]

Kyprolis is approved in the United States, Argentina, Israel, Kuwait, Mexico, Thailand, Colombia, Korea, Canada and the European Union. Additional regulatory applications for Kyprolis are underway and have been submitted to health authorities worldwide.

Kyprolis is a product of Onyx Pharmaceuticals, Inc. Onyx Pharmaceuticals is a subsidiary of Amgen and holds development and commercialization rights to Kyprolis globally, excluding Japan. For more information, please visit www.kyprolis.com.

Important EU Kyprolis® (carfilzomib) Safety Information

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Kyprolis treatment should be supervised by a physician experienced in the use of anti-cancer therapy. The most serious side effects that may occur during Kyprolis treatment include: Cardiac toxicity, pulmonary toxicities, pulmonary hypertension, dyspnea, hypertension including hypertensive crises, acute renal failure, tumor lysis syndrome, infusion reactions, thrombocytopenia, hepatic toxicity, posterior reversible encephalopathy syndrome (PRES) and thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS). The most common side effects are anemia, fatigue, diarrhea, thrombocytopenia, nausea, pyrexia, dyspnea, respiratory tract infection, cough and peripheral edema.

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

Important U.S. Safety Information Regarding Kyprolis® (carfilzomib) for Injection

INDICATION(S)

- KYPROLIS® (carfilzomib) is indicated 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.
- KYPROLIS® (carfilzomib) is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

IMPORTANT SAFETY INFORMATION

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred

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

Acute Renal Failure

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

Tumor Lysis Syndrome

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

Pulmonary Toxicity

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

Pulmonary Hypertension

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

Dyspnea

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

Hypertension

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

Venous Thrombosis

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

Infusion Reactions

- Infusion reactions, including life-threatening reactions, have occurred in patients receiving KYPROLIS. Symptoms include

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

Thrombocytopenia

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

Hepatic Toxicity and Hepatic Failure

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

Thrombotic Microangiopathy

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

Posterior Reversible Encephalopathy Syndrome (PRES)

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

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals.
- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

ADVERSE REACTIONS

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

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

About Aranesp® (darbepoetin alfa) in the U.S.

Aranesp is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.

Aranesp is indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Limitations of Use:

Aranesp has not been shown to improve quality of life, fatigue, or patient well-being.

Aranesp is not indicated for use:

- In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
- In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
- As a substitute for red blood cell transfusions in patients who require immediate correction of anemia.

Important EU Aranesp® Safety Information

Aranesp is indicated for treatment of symptomatic anemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy.

Aranesp is contraindicated in patients with poorly controlled hypertension.

As with all growth factors, there is a concern that epoetins could stimulate the growth of tumours. In several controlled studies, epoetins have not been shown to improve overall survival or decrease the risk of tumour progression in patients with anemia associated with cancer.

In controlled clinical studies, use of Aranesp and other ESAs have shown:

- Shortened time to tumour progression in patients with advanced head and neck cancer receiving radiation therapy when administered to target Hb > 14 g/dL; ESAs are not indicated for use in this patient population
- Shortened overall survival and increased deaths attributed to disease progression at 4 months in patients with metastatic breast cancer receiving chemotherapy when administered to target Hb 12-14 g/dL(7.5-8.7 mmol/l).
- Increased risk of death when administered to target Hb of 12 g/dl (7.5 mmol/l) in patients with active malignant disease receiving neither chemotherapy nor radiation therapy; ESAs are not indicated for use in this patient population.

In view of the above, in some clinical situations blood transfusion should be the preferred treatment for the management of anemia in patients with cancer. The decision to administer recombinant erythropoietins should be based on a benefit-risk assessment with the participation of the individual patient, which should take into account the specific clinical context. Factors that should be considered in this assessment should include the type of tumour and its stage; the degree of anemia; life-expectancy; the environment in which the patient is being treated; and patient preference.

In patients with solid tumours or lymphoproliferative malignancies, if Hb >12 g/dL (7.5 mmol/l), the dose should be reduced according to the instructions provided in the Summary of Product Characteristics to minimise the potential risk of thromboembolic events. Platelet counts and haemoglobin level should also be monitored at regular intervals.

Discontinue use after the end of chemotherapy.

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

Important U.S. Safety Information for Aranesp®(darbepoetin alfa)

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE

Chronic Kidney Disease:

- **In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.**
- **No trial has identified a hemoglobin target level, Aranesp® dose, or dosing strategy that does not increase these risks.**
- **Use the lowest Aranesp® dose sufficient to reduce the need for red blood cell (RBC) transfusions.**

Cancer:

- **ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.**
- **Because of these risks, prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology Program to prescribe and/or dispense Aranesp® to patients with cancer. To enroll in the ESA APPRISE Oncology Program, visit www.esa-apprise.com or call 1-866-284-8089 for further assistance.**
- **To decrease these risks, as well as the risk of serious cardiovascular and thromboembolic reactions, use the lowest dose needed to avoid RBC transfusions.**
- **Use ESAs only for anemia from myelosuppressive chemotherapy.**
- **ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure.**
- **Discontinue following the completion of a chemotherapy course.**

Aranesp is contraindicated in patients with uncontrolled hypertension, pure red cell aplasia (PRCA) that begins after treatment with Aranesp or other erythropoietin protein drugs, or serious allergic reactions to Aranesp.

Use caution in patients with CKD and coexistent cardiovascular disease and stroke. Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other patients. A rate of hemoglobin rise of > 1 g/dL over 2 weeks may contribute to these risks. In controlled clinical trials of patients with cancer, Aranesp and other ESAs increased the risks for death and serious adverse cardiovascular reactions. These adverse reactions included myocardial infarction and stroke. In controlled clinical trials, ESAs increased the risk of death in patients undergoing coronary artery bypass graft surgery (CABG) and the risk of deep venous thrombosis (DVT) in patients undergoing orthopedic procedures. Control hypertension prior to initiating and during treatment with Aranesp.

Aranesp increases the risk of seizures in patients with CKD. Monitor patients closely for new-onset seizures, premonitory symptoms, or change in

seizure frequency.

For lack or loss of hemoglobin response to Aranesp, initiate a search for causative factors. If typical causes of lack or loss of hemoglobin response are excluded, evaluate for PRCA. Cases of PRCA and of severe anemia, with or without other cytopenias that arise following the development of neutralizing antibodies to erythropoietin have been reported in patients treated with Aranesp. This has been reported predominantly in patients with CKD receiving ESAs by subcutaneous administration. PRCA has also been reported in patients receiving ESAs for anemia related to hepatitis C treatment (an indication for which Aranesp is not approved). If severe anemia and low reticulocyte count develop during treatment with Aranesp, withhold Aranesp and evaluate patients for neutralizing antibodies to erythropoietin. Permanently discontinue Aranesp in patients who develop PRCA following treatment with Aranesp or other erythropoietin protein drugs. Do not switch patients to other ESAs.

Serious allergic reactions, including anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria may occur with Aranesp. Immediately and permanently discontinue Aranesp® if a serious allergic reaction occurs.

Adverse reactions (≥ 10%) in Aranesp clinical studies in patients with CKD were hypertension, dyspnea, peripheral edema, cough, and procedural hypotension. Adverse reactions (≥ 1%) in Aranesp® clinical studies in cancer patients receiving chemotherapy were abdominal pain, edema, and thrombovascular events.

To see the Aranesp Prescribing Information, including Boxed Warnings, and Medication Guide visit www.aranesp.com.

About Nplate® (romiplostim)

Nplate is approved in over 50 countries worldwide, including the U.S., European Union (EU), Canada, Australia, Russia, Mexico, Switzerland, Lichtenstein, Japan, Argentina, Israel, South Korea, Hong Kong, and Chile. Nplate also has received orphan designation for chronic ITP in the U.S. (2003), the EU (2005) and other parts of the world.

Nplate is the first FDA-approved treatment specifically for adult chronic ITP

In the U.S., Nplate is indicated for the treatment of thrombocytopenia in patients with chronic ITP 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 chronic 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.

In the EU, Nplate is indicated for adult chronic-immune (idiopathic)-thrombocytopenic-purpura (ITP) patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).

Nplate was named as a recipient of the U.S. Prix Galien 2009 "Best Biotechnology Product" award and also received the 2009 Scrip Awards for "Best New Drug." Nplate has also been honored with numerous awards throughout the EU, including a 2010 Prix Galien in France in the category of "Drugs for Rare Diseases," and the 2011 Prix Galien in Germany in the category of "Specialist Care." In September 2010, Nplate was awarded the 2010 International Prix Galien Award, an award granted every two years which recognizes the "best of the best" selected from previous national Prix Galien award recipients.

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

Important EU Nplate® Safety Information

The EU Summary of Product Characteristics for Nplate lists the following Special Warnings and Precautions: Reoccurrence of thrombocytopenia and bleeding after cessation of treatment, increased bone marrow reticulin, thrombotic/thromboembolic complications, progression of existing MDS (in patients with MDS), medication errors, loss of response to Nplate, and effects on red and white blood cells.

The most common adverse reactions observed include hypersensitivity reactions (including cases of rash, urticarial and angioedema) and headache. As with all therapeutic proteins, there is a potential for immunogenicity.

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

Important U.S. Nplate® Safety Information

Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia

- In Nplate® 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 chronic 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.

Laboratory Monitoring

- Obtain CBCs, including platelet counts, weekly during the dose adjustment phase of
- Nplate® therapy and then monthly following establishment of a stable Nplate® dose.
- Obtain CBCs, including platelet counts, weekly for at least two weeks following discontinuation of Nplate®.

Adverse Reactions

- In the placebo-controlled trials, headache was the most commonly reported adverse drug reaction, occurring in 35% of patients receiving Nplate® and 32% of patients receiving placebo. Headaches were usually of mild or moderate severity.
- Most common adverse reactions (≥ 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%).
- 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.

Please see full U.S. Prescribing Information and Medication Guide at www.Nplate.com

About Amgen

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

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

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

About Amgen's Commitment to Oncology

Amgen Oncology is committed to helping patients take on some of the toughest cancers, such as those that have been resistant to drugs, those that progress rapidly through the body and those where limited treatment options exist. Amgen's supportive care treatments help patients combat certain side effects of strong chemotherapy, and our targeted medicines and immunotherapies focus on more than a dozen different malignancies, ranging from blood cancers to solid tumors. With decades of experience providing therapies for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including

biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock.

The scientific information discussed in this news release related to new indications for Amgen's 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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