New Analyses From Pivotal Phase 3 Studies Show Kyprolis® (Carfilzomib) Allows Patients With Relapsed Multiple Myeloma To Live Longer Without Disease Progression

June 10, 2016

Cumulative Rates of Complete Response or Better Increased Over Time in Patients Treated With Kyprolis in Combination With Lenalidomide and Dexamethasone (KRd)

In a Post-Hoc Analysis, Treatment With KRd for 18 Months Reduced Risk of Progression or Death by 42 Percent During That Period

Additional Analyses Showed Kyprolis Plus Dexamethasone (Kd) was Superior to Bortezomib Plus Dexamethasone (Vd) Across Patient Populations

THOUSAND OAKS, Calif., June 10, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced results from a post-hoc analysis of the pivotal Phase 3 ASPIRE study which highlighted the benefit of continued treatment with Kyprolis® (carfilzomib) in combination with lenalidomide and dexamethasone (KRd) in patients with relapsed multiple myeloma. Separate sub-analyses of the Phase 3 ENDEAVOR study further confirmed efficacy and depth of response benefits of Kyprolis plus dexamethasone (Kd). These results were presented at the 21st Congress of the European Hematology Association (EHA).

Results from the ASPIRE analysis showed that cumulative rates of complete response or better (≥CR) continued to increase over time in the KRd arm, most quickly in the first 15 months of treatment. In addition, the progression-free survival (PFS) hazard ratio (HR) at 18 months was 0.58 (95 percent CI: 0.46-0.72), while the overall study HR at 31 months was 0.69 (95 percent CI: 0.57-0.83), possibly related to patients in the KRd arm receiving Kyprolis for a maximum of 18 months (EHA abstract #P275). Researchers assessed PFS HR at 18 months following discontinuation of Kyprolis treatment in the KRd arm per the trial protocol. The most common all grade treatment-related adverse events in the ASPIRE trial included neutropenia (34.2 percent), anemia (25.5 percent), fatigue (22.4 percent) and thrombocytopenia (22.4 percent).

Six additional abstracts presented at EHA further demonstrate the benefit of Kyprolis-based regimens across a range of patient populations:

- Data analyzed in four presentations across patient subgroups from the Phase 3 ENDEAVOR trial showed that patients with relapsed or refractory multiple myeloma who were treated with Kd achieved superior PFS compared to those receiving bortezomib plus dexamethasone (Vd). The subgroup analyses evaluated the Kyprolis combination based on prior treatment, cytogenetic risk status, age and in Asian patients, respectively (EHA abstracts #E1266, #E1267, #E1274 and #E1328).
- A secondary analysis of data from the Phase 3 ENDEAVOR study found treatment with Kd compared to subcutaneous bortezomib led to prolonged PFS regardless of prior bortezomib treatment. The results suggest Kd has a favorable benefit-risk profile and delivers superior efficacy and improved clinical outcomes (EHA abstract #P659).
- A separate presentation analyzed the efficacy and safety of Kyprolis according to baseline cytogenetic risk status, based on data from the Phase 3 ASPIRE trial in which KRd demonstrated a significant improvement in PFS compared to lenalidomide and dexamethasone alone (EHA abstract #P663).

"This week's presentations at EHA continue to confirm that compared to previous standard of care therapies, across patient populations and therapeutic combinations, treatment with Kyprolis can extend the time patients live without their disease progressing," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "This abundant clinical research provides substantive, meaningful evidence for Kyprolis as a foundational therapy for relapsed or refractory multiple myeloma patients."

Abstracts are currently available on the EHA website.

EHA Abstract #P275:
Carfilzomib, Lenalidomide, and Dexamethasone Versus Lenalidomide and Dexamethasone in Patients with Relapsed Multiple Myeloma: Analysis of Response and Progression-Free Survival Hazard Ratio Over Time
In this post-hoc analysis of data from the Phase 3 ASPIRE trial, researchers evaluated the time to cumulative ≥CR and PFS HR at 18 months from randomization for KRd-treated patients (n=396) versus Rd-treated patients (n=396). KRd and Rd patients were followed for a median of 31 and 30 months for PFS, respectively. Per trial protocol, Kyprolis was discontinued after 18 cycles (28 days/cycle), so optimal duration of KRd treatment was not determined. All patients continued to receive Rd treatment until disease progression.

- A total of 126 and 37 patients in the KRd and Rd groups achieved ≥CR with sample median time from treatment start to ≥CR of 6.7 and 8.3 months, respectively. The increase in rate of ≥CR patients over time was greater in the KRd group than the Rd group, most notably in the first 15 months; cumulative ≥CR rates increased steadily thereafter.
- The overall PFS HR in ASPIRE for KRd versus Rd was 0.69 (95 percent CI: 0.57-0.83). For the first 18 months, the PFS HR was 0.58 (95 percent CI: 0.46-0.72). The 18-month PFS HR was lower than the overall study PFS HR, possibly related to KRd patients receiving Kyprolis for a maximum of 18 months.
- The most common all grade treatment-related adverse events in the ASPIRE trial included neutropenia (34.2 percent), anemia (25.5 percent), fatigue (22.4 percent) and thrombocytopenia (22.4 percent).

EHA Abstract #E1266: Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone: Subgroup Analysis of the Phase 3

ENDEAVOR Study to Evaluate the Impact of Prior Treatment on Patients with Relapsed Multiple Myeloma
This subgroup analysis evaluated treatment with Kd versus Vd in patients after first relapse versus more than two prior lines of therapy, as well as the effect of previous exposure to bortezomib or lenalidomide.

- For patients with prior bortezomib exposure, median PFS for Kd compared to Vd was 15.6 months versus 8.1 months, respectively (HR: 0.56; 95 percent CI: 0.44-0.73). For patients without prior bortezomib exposure, median PFS was not estimable (NE) for the Kd-treated patients versus 11.2 months for Vd-treated patients (HR: 0.48; 95 percent CI: 0.36-0.66). In patients with prior bortezomib exposure, overall response rates (ORRs) were 71.2 percent for Kd versus 60.3 percent for Vd (OR: 1.63; 95 percent CI: 1.12-2.36) and 83.6 percent for Kd compared to 65.3 percent for Vd (OR: 2.72; 95 percent CI: 1.72-4.31) in patients without prior bortezomib exposure.
- For patients with prior lenalidomide exposure, median PFS for Kd-treated patients was 12.9 months compared to 7.3 months for Vd-treated patients (HR: 0.69; 95 percent CI: 0.52-0.92). For patients without prior lenalidomide exposure, median PFS for Kd-treated patients was 22.2 months compared to 10.2 months for Vd-treated patients (HR: 0.43; 95 percent CI: 0.32-0.56). For patients with prior lenalidomide exposure, ORRs were 70.1 percent for Kd versus 59.3 percent for Vd (OR: 1.60; 95 percent CI: 1.03-2.49), and 81.2 percent for Kd versus 64.6 percent for Vd (OR: 2.37; 95 percent CI: 1.62-3.47) in patients without prior lenalidomide exposure.
- In patients with one prior line of therapy, grade 3 or higher adverse events were reported in 69.8 percent of patients in the Kd arm and 63.9 percent of patients in the Vd arm. In patients with two or more prior lines of therapy, grade 3 or higher adverse events were reported in 76.6 percent of patients in the Kd arm and 69.9 percent of patients in the Vd arm.

EHA Abstract #E1267: Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone: Subgroup Analysis of Patients with Relapsed Multiple Myeloma by Baseline Cytogenetic Risk Status (Phase 3 ENDEAVOR Study)
This pre-planned subgroup analysis evaluated the efficacy and safety outcomes in patients treated with Kd versus Vd according to patients' baseline cytogenetic risk status.

- In the high-risk group, median PFS was 8.8 months (95 percent CI: 6.9-11.3) for Kd-treated patients (n=97) versus 6.0 months for Vd-treated patients (n=113) (95 percent CI: 4.9-8.1) (HR: 0.646; 95 percent CI: 0.453-0.921). ORRs (≥ partial response) were 72.2 percent for Kd-treated patients versus 58.4 percent for Vd-treated patients. Median duration of response was 10.2 months for Kd versus 8.3 months for Vd.
- In the standard-risk group, median PFS was NE (95 percent CI: 18.7-NE) for Kd-treated patients (n=284) compared to 10.2 months (95 percent CI: 9.3-12.2) for Vd-treated patients (n=291) (HR: 0.439; 95 percent CI: 0.333-0.578). ORRs were 79.2 percent for Kd-treated patients versus 66.0 percent for Vd-treated patients. Median duration of response was NE for Kd versus 11.7 months for Vd.
- Grade 3 or higher adverse events were reported at higher rates with Kd versus Vd in both the high and standard-risk groups (70.1 percent versus 63.1 percent and 73.9 percent versus 68.3 percent, respectively).

EHA Abstract #E1274: Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone in Patients with Relapsed Multiple Myeloma: Analysis of the Phase 3 ENDEAVOR Study by Age Subgroup
This pre-planned subgroup analysis evaluated results of the ENDEAVOR study according to patients' age (younger than 65, 65-74, and 75 and older). Of the 929 patients enrolled, 223 patients received Kd and 210 received Vd in the <65 years subgroup; 164 patients received Kd and 189 received Vd in the 65-74 years subgroup; and 77 patients received Kd and 66 received Vd in the ≥75 years subgroup.

- For patients younger than 65 years, median PFS was NE for Kd-treated patients compared to 9.5 months for Vd-treated patients (HR: 0.58; 95 percent CI: 0.44-0.77). ORRs were 74 percent in the Kd arm versus 61 percent in the Vd arm (OR: 1.82; 95 percent CI: 1.21-2.74).
- For patients aged 65–74 years, median PFS was 15.6 months for Kd-treated patients versus 9.5 months for Vd-treated patients (HR: 0.53; 95 percent CI: 0.38-0.73). ORRs were 77 percent in the Kd arm versus 66 percent in the Vd arm (OR: 1.80; 95 percent CI: 1.12-2.89).
- For patients aged 75 years and older, median PFS was 18.7 months for Kd-treated patients versus 8.9 months for Vd-treated patients (HR: 0.38; 95 percent CI: 0.23-0.65). ORRs were 84 percent in the Kd arm versus 59 percent in the Vd arm (OR: 3.75; 95 percent CI: 1.71-8.24).
- Grade ≥3 hypertension, dyspnea, cardiac failure, renal failure were more common with Kd versus Vd. Deaths within 30 days post-study drug due to adverse events occurred.

EHA Abstract #E1328: Outcomes for Asian Patients With Relapsed Multiple Myeloma Treated With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone: A Subgroup Analysis of the Phase 3 ENDEAVOR Study
This pre-planned subgroup analysis evaluated the efficacy and safety outcomes in Asian patients (n=109) with relapsed multiple myeloma from the ENDEAVOR study. The majority of patients were from Japan (n=44; 40.4 percent), followed by Taiwan (n=24; 22.0 percent), Singapore (n=20; 18.3 percent), Republic of Korea (n=16; 14.7 percent), and Thailand (n=5; 4.6 percent).

- Median PFS follow-up was 8.4 months for Kd-treated patients and 7.6 months for Vd-treated patients. Median PFS was 14.9 months for Kd-treated patients (95 percent CI: 13.1-17.7) compared to 8.8 months for Vd-treated patients (95 percent CI: 6.6-NE) (HR: 0.57; 95 percent CI: 0.29-1.14), representing a greater than six month improvement.
- The ORR was 79.6 percent in the Kd arm (95 percent CI: 66.5-89.4) versus 70.9 percent in the Vd arm (95 percent CI:

57.1-82.4) (OR: 1.604; 95 percent CI: 0.664-3.872). The proportion of patients who achieved a best overall response of a ≥CR was higher in the Kd arm (9.3 percent) versus the Vd arm (1.8 percent). The rate of very good partial response (VGPR) or greater in the Kd arm (63.0 percent) was more than twice of that in the Vd arm (23.6 percent).
- Similar patient incidence rates of adverse events, grade 3 or higher adverse events, and grade 3 or higher treatment-related adverse events were observed between the Kd and Vd arms except for higher cardiovascular events and hypertension being observed in Kd arm.

EHA Abstract #P659: Carfilzomib and Dexamethasone Versus Subcutaneous Bortezomib and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma: Secondary Analysis from the Phase 3 Study ENDEAVOR

This subset analysis assessed the efficacy and safety of Kd compared to subcutaneous (SC) delivery of Vd, consistent with current standard of care, and the effect of prior exposure to bortezomib. The analysis compared Kd patients who had selected SC bortezomib delivery pre-randomization if randomized to the Vd arm (n=356) with Vd patients who used SC bortezomib (n=360).

- Median PFS has not been reached for patients treated with Kd but was 9.5 months for Vd patients treated with SC bortezomib (HR: 0.58; 95 percent CI: 0.46-0.72). Median overall survival has not been reached for Kd but was 24.3 months for SC Vd (HR: 0.75; 95 percent CI: 0.53-1.08). ORRs were 76.1 percent for Kd-treated patients compared to 64.4 percent for SC Vd-treated patients.
- For patients with prior bortezomib exposure, median PFS for Kd was 13.4 months compared to 8.4 months for SC Vd patients (HR: 0.66; 95 percent CI: 0.50-0.87). ORRs were 70.4 percent for Kd-treated patients and 62.1 percent for SC Vd-treated patients.
- Grade 3 or higher adverse events were 74.4 percent in the Kd arm and 67.5 percent in the SC Vd arm. For patients with prior bortezomib exposure, grade 3 or higher adverse events were 71.8 percent in the Kd arm compared to 64.5 percent in the SC Vd arm.

EHA Abstract #P663: 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

This pre-planned subgroup analysis assessed the efficacy and safety of KRd compared with lenalidomide and dexamethasone (Rd) according to baseline cytogenetic risk status in patients with relapsed multiple myeloma who had received one to three prior lines of therapy.

- For high-risk patients (n=100) treated with KRd, median PFS was 23.1 months (95 percent CI: 12.5-24.2) compared to 13.9 months (95 percent CI: 9.5-16.7) for patients treated with Rd (HR: 0.639; 95 percent CI: 0.369-1.106). ORRs were 79.2 percent for patients treated with KRd versus 59.6 percent for Rd-treated patients.
- In the standard risk group (n=317), median PFS was 29.6 months (95 percent CI: 24.1-NE) and 19.5 months (95 percent CI: 14.8-26.0), respectively (HR: 0.657; 95 percent CI: 0.480-0.901). ORRs for KRd-treated patients were 91.2 percent compared to 73.5 percent for patients treated with Rd.
- Rates of grade 3 or higher adverse events were 89.1 percent for KRd-treated patients compared to 78.4 percent for Rd-treated patients in the high-risk group, and 85.6 percent for KRd-treated patients versus 84.5 percent for Rd-treated patients in the standard risk group.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[1] It is a rare and very aggressive disease that accounts for approximately one percent of all cancers.[2-4] In Europe, approximately 39,000 patients are diagnosed with multiple myeloma each year and 24,000 patient deaths are reported on an annual basis.[2] Worldwide, more than 230,000 people are living with multiple myeloma.[2]

About Amgen's Commitment to Oncology

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

About Kyprolis® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[5] Kyprolis has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[5] In some cells, Kyprolis can cause cell death, especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[5,6]

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

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

Kyprolis is also approved in Argentina, Israel, Kuwait, Mexico, Thailand, Colombia, Korea, Canada, Switzerland, Russia 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 on Kyprolis in the U.S. please visit www.kyprolis.com.

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

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

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

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

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

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. 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 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 or the European Medicines Agency 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.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (Media)
Kristen Neese, 805-313-8267 (Media)
Arvind Sood, 805-447-1060 (Investors)

References

1. Jakubowiak A. Management Strategies for Relapsed/Refractory Multiple Myeloma: Current Clinical Perspectives. Seminars in Hematology. 2012; 49(3)(1),S16-S32.
2. GLOBCAN 2012, Global Prevalence and Incidence. Available at: http://globocan.iarc.fr/old/summary_table_pop_prev.asp?selection=224900&title=World&sex=0&window=1&sort=0&submit=%C2%A0Execute%C2%A0. Accessed on May 6, 2016.
3. American Cancer Society. Multiple myeloma. Available at: http://www.cancer.org/acs/groups/cid/documents/webcontent/003121-pdf.pdf. Accessed on: May 6, 2016.
4. Palumbo A and Anderson K, Multiple myeloma, *N Engl J Med*,2011;364:1046–60
5. Moreau P, Richardson PG, Cavo M et al. Proteasome Inhibitors in Multiple Myeloma: 10 Years Later. *Blood*. 2012; 120(5):947-959.
6. Kortuem KM and Stewart AK. Carfilzomib. *Blood*. 2012; 121(6):893-897.5.

Logo - http://photos.prnewswire.com/prnh/20081015/AMGENLOGO