FDA Approves New KYPROLIS® (carfilzomib) Combination Regimen With DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) and dexamethasone For Patients With Multiple Myeloma At First Or Subsequent Relapse

December 1, 2021

KYPROLIS in Combination With Subcutaneous Treatment Regimen Provides Further Options and Convenience for Patients With Relapsed/Refractory Multiple Myeloma

THOUSAND OAKS, Calif., Dec. 1, 2021 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved the expansion of the KYPROLIS® (carfilzomib) U.S. prescribing information to include its use in combination with DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.

"I am pleased that the addition of subcutaneous daratumumab to KYPROLIS plus dexamethasone will offer increased flexibility and convenience for patients with relapsed or refractory multiple myeloma and will greatly reduce the administration burden," said David M. Reese, M.D., executive vice president of Research and Development at Amgen.

The expansion of the KYPROLIS prescribing information to include DARZALEX *FASPRO* plus dexamethasone was supported by the ongoing, Phase 2, non-randomized, open-label, multicenter PLEIADES trial evaluating the clinical benefit of DARZALEX *FASPRO* administered in combination with four standard-of-care treatment regimens in patients with multiple myeloma.

Updated data from the PLEIADES study were presented at the 2020 American Society of Hematology (ASH) Annual Meeting, demonstrating that response rates with KYPROLIS in combination with DARZALEX *FASPRO* and dexamethasone were similar to those in the Phase 3 CANDOR study (KYPROLIS combined with intravenous [IV] DARZALEX and dexamethasone [DKd]), which supported the first-ever approval of an anti-CD38 monoclonal antibody in combination with KYPROLIS.[1] The PLEIADES study met its primary endpoint, demonstrating an overall response rate of 84.8 percent with DARZALEX *FASPRO*-Kd.

"Managing and coping with relapsed disease is a particularly challenging time in a patient's treatment journey, and having the option of subcutaneous daratumumab as part of the DKd treatment regimen will be a welcomed option for many of our patients," said Dr. Saad Usmani, M.D., chief of Myeloma Service at Memorial Sloan Kettering Cancer Center. "Administration time can be drastically reduced, as compared to the intravenous daratumumab formulation in combination with carfilzomib and dexamethasone."

Serious adverse reactions occurred in 27% of patients who received KYPROLIS in combination with DARZALEX *FASPRO* and dexamethasone. The most common adverse reactions (≥20%) were upper respiratory tract infection, fatigue, insomnia, hypertension, diarrhea, cough, dyspnea, headache, pyrexia, nausea and peripheral edema. Fatal adverse reactions occurred in 3% of patients.

Amgen will be submitting marketing applications globally.

About PLEIADES

The ongoing, Phase 2, non-randomized, open-label, multicenter PLEIADES trial evaluated the clinical benefit of DARZALEX *FASPRO* administered in combination with four standard-of-care treatment regimens in patients with multiple myeloma. The efficacy of KYPROLIS in combination with DARZALEX *FASPRO* and dexamethasone was evaluated in 66 patients with relapsed or refractory multiple myeloma in a single-arm cohort of PLEIADES.

KYPROLIS was evaluated at a starting dose of 20 mg/m^2 on Cycle 1 Day 1, which was increased to 70 mg/m^2 as a 30-minute IV infusion on Cycle 1 Day 8 and Day 15, and then Day 1, 8 and 15 of each cycle; DARZALEX *FASPRO* 1,800 mg administered subcutaneously once weekly from Weeks 1 to 8, once every 2 weeks from Weeks 9 to 24 and once every 4 weeks starting with Week 25 until disease progression or unacceptable toxicity; and dexamethasone 40 mg per week.

For more information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT03412565.

About CANDOR

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

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

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

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[2] It is a rare and life-threatening disease that accounts for approximately one percent of all cancers. [2,3] Worldwide, approximately 176,000 people are diagnosed with multiple myeloma each

year, and 117,000 patient deaths are reported on an annual basis.[3]

About KYPROLIS® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[4] KYPROLIS has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[5] In some cells, KYPROLIS can cause cell death, especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[4,5]

Since its first approval in 2012, approximately 200,000 patients worldwide have received KYPROLIS.[6]

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

- for the treatment of adult 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; or
  - Daratumumab and hyaluronidase-fihj 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, China, 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 Arabi, Serbia, Singapore, S. Africa, S. Korea, Switzerland, Taiwan, Thailand, Turkey, United Arab Emirates, and the United Kingdom.

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

Acute Renal Failure

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

Tumor Lysis Syndrome

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

Pulmonary Toxicity

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

Pulmonary Hypertension

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

Dyspnea

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

Hypertension

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

Venous Thrombosis

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

Infusion Reactions

- Infusion reactions, including life–threatening reactions, have occurred. 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.

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

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

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman.
- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS and for 3 months following the final dose. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Adverse Reactions

- The most common adverse reactions in the combination therapy trials: anemia, 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 at www.kyprolis.com.

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.

Amgen Forward-Looking Statements
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of 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, outcomes, progress, or effects relating to studies of Otezla as a potential treatment for COVID-19, 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.

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