Amgen Initiates Phase 3 Study Evaluating Once-Weekly Kyprolis® (carfilzomib) in Patients With Relapsed And Refractory Multiple Myeloma

May 31, 2015

Data from Once-Weekly CHAMPION Phase 1/2 Study Presented at ASCO

THOUSAND OAKS, Calif., May 31, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the initiation of the ARROW trial, a global Phase 3 study evaluating the benefit of Kyprolis® (carfilzomib) for Injection administered once-weekly with dexamethasone versus the current U.S. Food and Drug Administration (FDA) approved twice-weekly administration schedule in patients with relapsed and refractory multiple myeloma who have received prior treatment with bortezomib and an immunomodulatory agent (IMiD). The trial was initiated based on results from the Phase 1/2 CHAMPION study, which were presented (abstract no. 8527) at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) on Sunday, May 31 at 8 a.m. CT.

Results from the Phase 1 and 2 portions of CHAMPION were presented for 104 patients (Phase 1, n=15; Phase 2, n=89) with relapsed or refractory multiple myeloma who had received one to three prior treatment regimens at the determined maximum tolerated dose (MTD) of 20/70 mg/m^2. In the Phase 2 portion of the study, the overall response rate (ORR; defined as the percentage of patients achieving a partial response or better) was 77 percent. The clinical benefit rate (CBR; defined as the percentage of patients with minimal response or better) was 84 percent; the median time to response for patients who achieved a partial response or better was 1.6 months (range, 0.7-7.2); Kaplan-Meier median duration of response (DOR) was 15 months (95 percent CI 9-not estimable); and the Kaplan-Meier median progression-free survival (PFS) was 10.6 months (95 percent CI 9.0-16.1).

"The results from the CHAMPION Phase 1/2 study form the basis of the Phase 3 ARROW study with the goal of potentially providing patients and physicians greater convenience with a once-weekly dosing schedule of Kyprolis," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The initiation of this trial underscores our commitment to addressing the needs of patients with multiple myeloma through the entire treatment continuum."

The most common hematologic treatment-emergent adverse events (AEs) of any grade were anemia (24 percent), thrombocytopenia (22 percent) and neutropenia (8 percent). The most common non-hematologic treatment-emergent AEs of any grade were fatigue (52 percent), nausea (35 percent), headache and diarrhea (31 percent each). The most commonly occurring grade ≥3 hematologic treatment-emergent AEs were thrombocytopenia (6 percent), anemia (5 percent) and neutropenia (4 percent). The most common non-hematologic grade ≥3 treatment-emergent AEs were fatigue (11 percent), pneumonia (7 percent), acute renal failure and hypertension (6 percent each). Adverse events grade ≥3 included cardiac failure (2 percent) and peripheral neuropathy (1 percent).

A total of 36 patients (35 percent) had at least one serious AE. Sixteen patients (15 percent) treated at the MTD had at least one carfilzomib dose reduction due to AEs, and 10 patients (10 percent) discontinued study treatment due to AEs. Ten patients (10 percent) discontinued treatment due to investigator's discretion, 12 patients (12 percent) discontinued due to patient decision and 34 patients (33 percent) discontinued due to progressive disease. A total of five patients died during the study, all of which were in the Phase 2 portion of the study: one patient each had cause of death reported as cardiopulmonary arrest, pneumonia, disease progression, acute respiratory distress syndrome and acute kidney injury.

About CHAMPION

The CHAMPION (**C**ommunity **H**armonized **A**ssessment of **M**yeloma **P**atients via an **I**ntegrated **O**ncology **N**etwork) trial is a Phase 1/2, multicenter, single-arm, non-randomized, open-label and dose-escalation study of weekly Kyprolis with dexamethasone for patients with relapsed or refractory multiple myeloma. The primary objective of the Phase 1 portion of the study was to determine the MTD of once-weekly Kyprolis with dexamethasone. The primary objective of the Phase 2 portion of the study was to determine the ORR. Secondary endpoints were to evaluate the CBR, PFS, time to progression and DOR. Patients who received one to three prior treatment regimens were eligible to enroll. The last patient was enrolled in September 2014, and the data cutoff date for analyses presented at ASCO was May 1, 2015. A total of 48 percent of enrolled patients were bortezomib-refractory, 28 percent were lenalidomide-refractory and 16 percent were refractory to both bortezomib and lenalidomide. In the Phase 1 portion, patients received Kyprolis as a 30-minute intravenous (IV) infusion on days 1, 8 and 15 of a 28-day cycle using a standard 3+3 dose-escalation scheme. Patients received Kyprolis at 20 mg/m^2 on day 1 of cycle 1. Subsequent doses started at 45 mg/m^2 and were escalated to 56, 70 or 88 mg/m^2 beginning on day 8 of cycle 1 until the MTD of 20/70 mg/m^2 was reached for use in the Phase 2 portion. Patients received dexamethasone 40 mg (IV or oral) on days 1, 8, 15 and 22 of cycles 1–8; dexamethasone was omitted on day 22 beginning in cycle 9. Treatment was administered until disease progression or unacceptable toxicity was observed.

For more information about CHAMPION, please visit www.clinicaltrials.gov under trial identification number NCT01677858.

About ARROW

The ARROW (R**A**ndomized, Open-label, Phase 3 Study in Subjects with **R**elapsed and **R**efractory Multiple Myeloma Receiving Carfilzomib in Combination with Dexamethasone, Comparing **O**nce-**W**eekly versus Twice-weekly Carfilzomib Dosing) trial is evaluating approximately 460 patients with relapsed and refractory multiple myeloma who have received at least two but no more than three prior therapies, including bortezomib and an IMiD. Those included in the study will be randomized to receive once-weekly Kyprolis (20 mg/m^2 on day 1 of cycle 1, 70 mg/m^2 on days 8 and 15 of cycle 1 and 70 mg/m^2 on days 1, 8 and 15 of subsequent cycles) with dexamethasone (40 mg) versus twice-weekly Kyprolis (20 mg/m^2 on days 1 and 2 of cycle 1, 27 mg/m^2 on days 8, 9, 15 and 16 of cycle 1 and 27 mg/m^2 on days 1, 2, 8, 9, 15 and 16 of subsequent cycles) with dexamethasone (40 mg). The primary endpoint of the trial is ORR, defined as the proportion of subjects achieving a best overall response of partial response, very good partial response, complete response or stringent complete response based on the International Myeloma Working Group Uniform Response Criteria. Secondary endpoints include PFS, overall survival and safety and tolerability. The trial is being conducted in approximately 100 sites worldwide. For more information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT02412878.

About Multiple Myeloma

Multiple myeloma is the second most common hematologic cancer and results from an abnormality of plasma cells, usually in the bone marrow.[1,2] Worldwide, nearly 230,000 people are living with multiple myeloma and approximately 114,000 new cases are diagnosed annually.[3] In the U.S., there are nearly 96,000 people living with, or in remission from, multiple myeloma. The estimated number of new cases of multiple myeloma in 2014 was more than 24,000 and the estimated number of deaths was 11,090.[4] In Europe, approximately 89,000 people are living with the disease and in 2012 there was an estimated 39,000 newly diagnosed cases and 24,000 deaths.[3]

Amgen Post-ASCO Summary Webcast

Amgen will hold a post-ASCO summary webcast on Tuesday, June 2 at 1 p.m. CT. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, along with members of Amgen's clinical development team and clinical investigators will participate to discuss data presented at ASCO and Amgen's broader oncology portfolio of products.

Live audio of the event will be simultaneously broadcast over the Internet and will be available to members of the news media, investors and the general public.

The webcast, as with other selected presentations regarding developments in Amgen's business given by management at certain investor and medical conferences, can be found on Amgen's website, www.amgen.com, under Investors. Information regarding presentation times, webcast availability and webcast links are noted on Amgen's Investor Relations Events Calendar. The webcast will be archived and available for replay for at least 90 days after the event.

About Kyprolis® (carfilzomib) for Injection

On July 20, 2012, the U.S. FDA granted accelerated approval of Kyprolis® (carfilzomib) for Injection for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent (IMiD) and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval was based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified. Kyprolis is also approved for use in Argentina, Israel and Mexico.

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 about Kyprolis, visit www.kyprolis.com.

Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection

This safety information is specific to the current U.S. approved indication, which is based on Phase 2 studies.

Safety data have been evaluated in 526 patients with relapsed and/or refractory multiple myeloma who received single-agent Kyprolis. There were 37 deaths in the Phase 2 studies, or 7 percent of patients. The most common causes of death, other than disease progression, were cardiac (5 patients), end-organ failure (4 patients) and infection (4 patients). Important warnings and precautions include cardiac arrest, congestive heart failure, myocardial ischemia, pulmonary hypertension, pulmonary complications, infusion reactions, tumor lysis syndrome, thrombocytopenia, hepatic toxicity and embryo-fetal toxicity.

Death due to cardiac arrest has occurred within a day of Kyprolis administration. Patients with New York Heart Association Class III and IV heart failure, myocardial infarction in the preceding 6 months and conduction abnormalities uncontrolled by medications were not eligible for the clinical trials. These patients may be at greater risk for cardiac complications.

Pulmonary arterial hypertension (PAH) was reported in 2 percent of patients treated with Kyprolis and was Grade 3 or greater in less than 1 percent of patients. Dyspnea was reported in 35 percent of patients enrolled in clinical trials. Grade 3 dyspnea occurred in 5 percent; no Grade 4 events and 1 death (Grade 5) was reported.

Infusion reactions, characterized by a spectrum of systemic symptoms including fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina can occur immediately following or up to 24 hours after administration of Kyprolis. Administration of dexamethasone prior to Kyprolis reduces the incidence and severity of reactions. Tumor lysis syndrome (TLS) occurred following Kyprolis administration in <1 percent of patients. Patients with multiple myeloma and a high tumor burden should be considered to be at greater risk for TLS.

Thrombocytopenia following Kyprolis administration resulted in a dose reduction in 1 percent of patients and discontinuation of treatment with Kyprolis in <1 percent of patients.

Cases of hepatic failure, including fatal cases, have been reported (<1 percent). Kyprolis can cause elevations of serum transaminases and bilirubin.

Cases of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) including fata outcome have been reported. Treatment with Kyprolis should be discontinued if signs and symptoms of TTP/HUS occur.

Cases of posterior reversible encephlophay syndrome (PRES) have been reported. Treatment with Kyprolis should be discontinued if PRES is suspected.

There are no adequate and well-controlled studies in pregnant women using Kyprolis. Females of reproductive potential should be advised to avoid becoming pregnant while being treated with Kyprolis.

The most common serious adverse reactions were pneumonia, acute renal failure, pyrexia and congestive heart failure. The most common adverse reactions (incidence of 30 percent or greater) observed in clinical trials of patients with multiple myeloma were fatigue, anemia, nausea, thrombocytopenia, dyspnea, diarrhea and pyrexia. Serious adverse reactions were reported in 45 percent of patients.

Full prescribing information is available 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 biologics manufacturing 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 Inc. and its subsidiaries (Amgen) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. 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 (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of May 31, 2015, and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. 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 Amgen and its partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Amgen depends on third parties for a significant portion of its manufacturing capacity for the supply of certain of its current and future products and limits on supply may constrain sales of certain of its current products and product candidate development.

In addition, sales of Amgen's products (including products of Amgen's wholly-owned subsidiaries) are affected by the 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 as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to some of its marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with its products. In addition, while Amgen and its partners routinely obtain patents for their products and technology, the protection of Amgen's products offered by patents and patent applications may be challenged, invalidated or circumvented by its competitors and there can be no guarantee of Amgen's or its partners' ability to obtain or maintain patent protection for Amgen's products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations. Amgen's efforts to integrate the operations of companies it has acquired may not be successful. Amgen may experience difficulties, delays or unexpected costs and not achieve anticipated cost savings from its recently announced restructuring plan. Amgen's business performance could affect or limit the ability of Amgen's Board of Directors to declare a dividend or their ability to pay a dividend or repurchase Amgen common stock.

The scientific information discussed in this news release relating 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.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (Media)
Trish Hawkins, 805-447-5631 (Media)
Arvind Sood, 805-447-1060 (Investors)

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