Amgen Announces First Clinical Data Evaluating Novel Investigational KRASG12C Inhibitor AMG 510 At ASCO 2019

June 3, 2019

AMG 510 is the First KRASG12C Inhibitor to Reach Clinical Stage After Three Decades of RAS Research

First-In-Human Results Show Preliminary Safety, Tolerability Data and Anti-Tumor Activity in KRAS Mutant Solid Tumors

FDA Grants AMG 510 Orphan Drug Designation for KRASG12C-Positive Non-Small Cell Lung and Colorectal Cancers

THOUSAND OAKS, Calif., June 3, 2019 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced the first clinical results from a Phase 1 study evaluating investigational AMG 510, the first $KRAS^{G12C}$ inhibitor to reach the clinical stage. In the trial, there were no dose-limiting toxicities at tested dose levels. AMG 510 showed anti-tumor activity when administered as a monotherapy in patients with locally-advanced or metastatic $KRAS^{G12C}$ mutant solid tumors. These data are being presented during an oral session at the 55th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

"KRAS has been a target of active exploration in cancer research since it was identified as one of the first oncogenes more than 30 years ago, but it remained undruggable due to a lack of traditional small molecule binding pockets on the protein. AMG 510 seeks to crack the KRAS code by exploiting a previously hidden groove on the protein surface," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "By irreversibly binding to cysteine 12 on the mutated KRAS protein, AMG 510 is designed to lock it into an inactive state. With high selectivity for $KRAS^{G12C}$, we believe investigational AMG 510 has high potential as both a monotherapy and in combination with other targeted and immune therapies."

The Phase 1, first-in-human, open-label multicenter study enrolled 35 patients with various tumor types (14 non-small cell lung cancer [NSCLC], 19 colorectal cancer [CRC] and two other). Eligible patients were heavily pretreated with at least two or more prior lines of treatment, consistent with their tumor type and stage of disease. The primary endpoint is safety, and key secondary endpoints include pharmacokinetics, objective response rate (assessed every six weeks), duration of response and progression-free survival. Patients were enrolled in four dose cohorts - 180 mg, 360 mg, 720 mg and 960 mg, taken orally once a day.

Five out of 10 evaluable patients with NSCLC experienced a partial response (PR), and another four had stable disease (SD), for a disease control rate (DCR) of 90 percent (9/10).[1] All five patients with response to therapy had a treatment duration of 7.3-27.4 weeks at data cutoff and remain active on treatment. One patient with PR improved further to a complete response of the target lesions at week 18, post data cutoff.

In addition, 13 of 18 evaluable patients with CRC achieved SD, with the majority of CRC patients treated at the first two dose levels. Twenty-six patients remain on study and nine have discontinued.

Treatment-related adverse events (AEs) were primarily grade 1 events (approximately 68 percent). Two grade 3 treatment-related AEs were reported (anemia and diarrhea). No grade 4 treatment-related AEs and no serious treatment-related AEs were reported. Enrollment into dose expansion is underway.

"While there's been significant progress in treating solid tumor cancers overall with targeted therapies, patients with the $KRAS^{G12C}$ mutation have not benefited from these advances," said Marwan G. Fakih, M.D., clinical study investigator and co-director of the Gastrointestinal Cancer Program, City of Hope, Duarte, Calif. "In this early Phase 1 trial, investigational AMG 510 showed encouraging anti-tumor activity. We look forward to further investigating AMG 510 with the goal of closing the treatment gap for patients with this type of mutation."

Amgen Webcast Investor Meeting
Amgen will host a webcast investor meeting at ASCO 2019 on Monday, June 3 at 6:30 p.m. CT. David M. Reese, 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 at the investor meeting to discuss Amgen's oncology program and data presented at ASCO 2019. Live audio of the conference call will be broadcast over the internet simultaneously 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 at certain investor and medical conferences, can be accessed 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 *KRAS*
The subject of more than three decades of research, the RAS gene family are the most frequently mutated oncogenes in human cancers.[2,3] Within this family, KRAS is the most prevalent variant and is particularly common in solid tumors.[3] A specific mutation known as $KRAS^{G12C}$ accounts for approximately 13 percent of non-small cell lung cancers, three to five percent of colorectal cancers and one to two percent of numerous other solid tumors.[4] Approximately 30,000 patients are diagnosed each year in the United States with $KRAS^{G12C}$ driven cancers.[5]Amgen is exploring the potential of $KRAS^{G12C}$ inhibition across a broad variety of tumor types.

About Amgen Oncology
Amgen Oncology is searching for and finding answers to incredibly complex questions that will advance care and improve lives for cancer patients and their families. Our research drives us to understand the disease in the context of the patient's life – not just their cancer journey – so they can take control of their lives.

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 are driven by our commitment to transform the lives of cancer patients and keep them at the center of everything we do.

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.

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 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. 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. 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 acquire other companies or products and to integrate the operations of companies 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. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

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

References

1. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *European Journal of Cancer*. 2009;45:228-247.
2. Cox A, et al. Drugging the undruggable RAS: Mission Possible? *Nature Reviews Drug Discovery*. 2014;13(11):828-851.
3. Fernandez-Medarde A, Santos E. Ras in Cancer and Developmental Diseases. *Genes Cancer*. 2011;2(3):344-358.
4. Lipford, JR. Pre-clinical development of AMG 510: the first inhibitor of KRASG12C in clinical testing. Oral presentation at AACR 2019; Atlanta, GA.March 29-April 3, 2019.
5. Stephen AG, et al. Dragging Ras Back in the Ring. Cancer Cell. 2014;25:272-281.

View original content to download multimedia:http://www.prnewswire.com/news-releases/amgen-announces-first-clinical-data-evaluating-novel-investigational-krasg12c-inhibitor-amg-510-at-asco-2019-300860318.html

SOURCE Amgen