Amgen Presents New Data From Thoracic Oncology Portfolio At WCLC21

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New LUMAKRAS™ (sotorasib) Post-Hoc Analysis Shows Intracranial Disease Control was Achieved in a Subset of Patients With Previously Treated Evaluable Stable Brain Metastases

Additional Featured Research Includes Exploratory Analysis of Potential Genomic Determinants of LUMAKRAS Response

THOUSAND OAKS, Calif., Sept. 8, 2021 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced results from two analyses of the Phase 2 CodeBreaK 100 clinical trial evaluating LUMAKRAS™ (sotorasib), the first and only $KRAS^{G12C}$ inhibitor approved in the U.S., in the treatment of previously treated patients with advanced or metastatic *KRAS* G12C-mutated non-small cell lung cancer (NSCLC). These new analyses, respectively, provide encouraging evidence of durable systemic anticancer activity in patients with previously treated, stable brain metastases with LUMAKRAS, as well as insights into biomarkers of LUMAKRAS response. Together with a poster describing a recently initiated clinical study of the investigational half-life extended (HLE) bispecific T cell engager (BiTE®) molecule acapatamab (formerly AMG 160) in patients with NSCLC, these data are being featured during the virtual 2021 World Conference on Lung Cancer (WCLC21) hosted by the International Association for the Study of Lung Cancer (IASLC).

"Amgen is expanding the reach, impact and potential of our innovative therapies to personalize care for patients with historically difficult-to-treat cancers like lung cancer," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "We are pleased to present additional analyses for LUMAKRAS, our newly approved $KRAS^{G12C}$ inhibitor, as well as a trial-in-progress poster for acapatamab, our investigational BiTE molecule being studied in NSCLC and other solid tumors. Of the data presented at WCLC, we are particularly encouraged by the first evaluation of LUMAKRAS' ability to maintain stabilization of brain metastases in patients with previously treated, stable brain metastases. We look forward to the results from our CodeBreaK 101 study where we are studying a cohort of *KRAS* G12C-mutated NSCLC patients with untreated, active brain metastases to better understand the clinical benefit of LUMAKRAS."

New Analyses From the LUMAKRAS Phase 2 CodeBreaK 100 Clinical Trial

In a post-hoc analysis (WCLC21 Poster 52.03) of 40 patients (23% of 174 trial participants) with *KRAS* G12C-mutated advanced NSCLC who had stable, previously treated brain metastases at their enrollment in the CodeBreaK 100 trial, LUMAKRAS achieved a 77.5% disease control rate (DCR), a median progression-free survival (PFS) of 5.3 months and a median overall survival (OS) of 8.3 months. This DCR was similar to patients without brain metastases. In patients evaluable by Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) criteria, 14 of 16 patients (88%) maintained intracranial disease control of their stable brain lesions during LUMAKRAS therapy with two achieving complete responses of non-target lesions. The safety profile of LUMAKRAS in the brain metastases group was consistent with previous reports. Amgen is enrolling patients with active brain metastases in an arm of the CodeBreaK 101 study (NCT04185883).

"Up to 40% of patients with *KRAS* G12C-mutated NSCLC may develop brain metastases.[1] Given the overall poor prognosis for this patient subset, there is an urgent need for novel treatment options,"[2] said lead author Suresh S. Ramalingam, M.D., executive director of Winship Cancer Institute of Emory University in Atlanta. "Our results demonstrate the potential of sotorasib to provide meaningful clinical benefit for *KRAS* G12C-mutated NSCLC in the brain."

An additional exploratory descriptive analysis of CodeBreaK 100 being presented during a Mini Oral Presentation (MA14.03) examined whether the mutation profile of the tumors, in addition to $KRAS^{G12C}$, is correlated with patients' responses or resistance to LUMAKRAS. An analysis of baseline tumor samples from 65 patients revealed no single genetic signature that predicted LUMAKRAS responses and ongoing evaluations will be needed to further identify potential targetable mechanisms of resistance. However, the *KEAP1* mutation, a known driver of poor clinical outcomes, was observed in 7 of 22 patients with early progression and PFS of less than 3 months.

"The introduction of sotorasib ushered in a new standard of care for patients with *KRAS* G12C-mutated NSCLC," said lead author Ferdinandos Skoulidis, M.D., Ph.D., assistant professor of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center. "These biomarker data provide direction for continued research into characterizing mutation profiles associated with sotorasib treatment response to help guide clinical practice and inform innovative combination approaches to overcome potential mechanisms of resistance."

Advancing BiTE Molecule Acapatamab in NSCLC

In addition to the LUMAKRAS data, a trial-in-progress abstract outlined the design of an ongoing open-label, Phase 1b study (NCT04822298) evaluating the safety and tolerability of acapatamab, a half-life extended BiTE immuno-oncology therapy that targets prostate specific membrane antigen (PSMA)-expressing cancer cells in adults with relapsed/refractory NSCLC. The encouraging benefit-risk profile of acapatamab in an ongoing trial of patients with metastatic castration-resistant prostate cancer (mCRPC) (NCT03792841) suggested its potential for patients with NSCLC, as up to 49 to 85% of the endothelial cells in a tumor's newly grown blood supply express PSMA.[3,4] Acapatamab engages PSMA on cancer cells and CD3 on T cells, inducing T-cell activation, proliferation and target cell lysis to prompt a cancer-fighting immune response.[5]

About LUMAKRAS™ (sotorasib)

Amgen took on one of the toughest challenges of the last 40 years in cancer research by developing LUMAKRAS, a $KRAS^{G12C}$ inhibitor.[6] LUMAKRAS has demonstrated a positive benefit-risk profile with rapid, deep and durable anticancer activity in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring the *KRAS* G12C mutation with a once daily oral formulation.[7]

In May 2021, LUMAKRAS was the first $KRAS^{G12C}$ inhibitor to receive regulatory approval anywhere in the world with its approval in the U.S., under accelerated approval. LUMAKRAS is also approved in the United Arab Emirates.

Amgen is progressing the largest and broadest global $KRAS^{G12C}$ development program with unparalleled speed and exploring more than 10 sotorasib combination regimens, including triplets, with clinical trial sites spanning five continents. To date, LUMAKRAS has treated almost 3,000

patients around the world through the clinical development program and commercial use.

In the U.S., LUMAKRAS was reviewed by the FDA under its Real-Time Oncology Review (RTOR), a pilot program that aims to explore a more efficient review process that ensures safe and effective treatments are made available to patients as early as possible. Amgen is participating in the FDA's Project Orbis initiative and through the initiative, has submitted Marketing Authorization Applications (MAAs) for sotorasib in Australia, Brazil, Canada and the United Kingdom. Additionally, Amgen has submitted an MAA in the EU and New Drug Applications in Japan (J-NDA), Switzerland, South Korea, Singapore, Israel, Turkey and Taiwan.

LUMAKRAS is also being studied in multiple other solid tumors.[6]

LUMAKRAS™ (sotorasib) U.S. Indication
LUMAKRAS™ is indicated for the treatment of adult patients with *KRAS* G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

LUMAKRAS™ (sotorasib) Important Safety Information

Hepatotoxicity

- LUMAKRAS™ can cause hepatotoxicity, which may lead to drug-induced liver injury and hepatitis.
- Among 357 patients who received LUMAKRAS™ in CodeBreaK 100, hepatotoxicity occurred in 1.7% (all grades) and 1.4% (Grade 3). A total of 18% of patients who received LUMAKRAS™ had increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST); 6% were Grade 3 and 0.6% were Grade 4. In addition to dose interruption or reduction, 5% of patients received corticosteroids for the treatment of hepatotoxicity.
- Monitor liver function tests (ALT, AST and total bilirubin) prior to the start of LUMAKRAS™, every 3 weeks for the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop transaminase and/or bilirubin elevations.
- Withhold, dose reduce or permanently discontinue LUMAKRAS™ based on severity of adverse reaction.

Interstitial Lung Disease (ILD)/Pneumonitis

- LUMAKRAS™ can cause ILD/pneumonitis that can be fatal. Among 357 patients who received LUMAKRAS™ ir CodeBreaK 100, ILD/pneumonitis occurred in 0.8% of patients, all cases were Grade 3 or 4 at onset, and 1 case was fatal. LUMAKRAS™ was discontinued due to ILD/pneumonitis in 0.6% of patients.
- Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold LUMAKRAS™ in patients with suspected ILD/pneumonitis and permanently discontinue LUMAKRAS™ if no other potential causes of ILD/pneumonitis are identified.

Most Common Adverse Reactions

- The most common adverse reactions ≥ 20% were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity and cough.

Drug Interactions

- Advise patients to inform their healthcare provider of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, dietary and herbal products.
- Inform patients to avoid proton pump inhibitors and H_2 receptor antagonists while taking LUMAKRAS™.
- If coadministration with an acid-reducing agent cannot be avoided, inform patients to take LUMAKRAS™ 4 hours before or 10 hours after a locally acting antacid.

Please see LUMAKRAS™ full Prescribing Information.

About Non-Small Cell Lung Cancer and the *KRAS* G12C Mutation
Lung cancer is the leading cause of cancer-related deaths worldwide, and it accounts for more deaths worldwide than colon cancer, breast cancer and prostate cancer combined.[8] Overall survival rates for NSCLC are improving but remain poor for patients with advanced disease and 5-year survival is only 7% for those with metastatic disease.[9]

KRAS G12C is the most common *KRAS* mutation in NSCLC.[10] In the U.S., about 13% of patients with non-squamous NSCLC harbor the *KRAS* G12C mutation.[11] Unmet medical need remains high and treatment options are limited for NSCLC patients with the *KRAS* G12C mutation whose first-line treatment has failed to work or has stopped working. The outcomes with current therapies are suboptimal with a median progression-free survival of approximately 4 months following second-line treatment of *KRAS* G12C-mutated NSCLC.[12]

About CodeBreaK
The CodeBreaK clinical development program for Amgen's drug sotorasib is designed to treat patients with an advanced solid tumor with the *KRAS* G12C mutation and address the longstanding unmet medical need for these cancers. As the most advanced *KRAS* G12C clinical development program, CodeBreaK has enrolled more than 800 patients across 13 tumor types since its inception.

CodeBreaK 100, the Phase 1 and 2, first-in-human, open-label multicenter study, enrolled patients with *KRAS* G12C-mutant solid tumors. Eligible patients must have received a prior line of systemic anticancer therapy, consistent with their tumor type and stage of disease. The primary endpoint for the Phase 2 study was centrally assessed objective response rate. The Phase 2 trial in NSCLC enrolled 126 patients, 124 of whom had centrally evaluable lesions by RECIST at baseline. The Phase 2 trial in colorectal cancer (CRC) is fully enrolled and results have been submitted for publication.

A global Phase 3 randomized active-controlled study comparing sotorasib to docetaxel in patients with *KRAS* G12C-mutated NSCLC (CodeBreaK 200) has completed enrollment. Amgen also has several Phase 1b studies investigating sotorasib monotherapy and sotorasib combination therapy across various advanced solid tumors (CodeBreaK 101) open for enrollment. A Phase 2 randomized study will evaluate sotorasib in patients with stage IV *KRAS* G12C-mutated NSCLC in need of first-line treatment (CodeBreaK 201).

For information, please visit www.hcp.codebreaktrials.com.

About BiTE® Technology

BiTE® (bispecific T cell engager) technology is a targeted immuno-oncology platform that is designed to engage a patient's own T cells to any tumor-specific antigen, activating the cytotoxic potential of T cells to eliminate detectable cancer. The BiTE immuno-oncology platform has the potential to treat different tumor types through tumor-specific antigens. The BiTE platform has a goal of leading to off-the-shelf solutions, which have the potential to make innovative T cell treatment available to all providers when their patients need it. Amgen is advancing BiTE molecules across a broad range of hematologic malignancies and solid tumors and further investigating BiTE technology with the goal of enhancing patient experience and therapeutic potential.

About Acapatamab (formerly AMG 160)

Acapatamab is a half-life extended (HLE) BiTE immune-oncology therapy that targets PSMA-expressing cancer cells being investigated in prostate cancer and non-small cell lung cancer (NSCLC).

Simultaneously binding to PSMA on tumor cells and CD3 on T cells, acapatamab is designed to engage patients' own T cells to fight cancer. In an ongoing Phase I, first-in-human study in patients with metastatic castration-resistant prostate cancer (mCRPC), acapatamab has demonstrated a manageable safety profile and promising efficacy as monotherapy.[3]

The mCRPC study is also examining acapatamab in combination with pembrolizumab. A Phase 1/2, master protocol study is investigating the safety, tolerability, dosing and efficacy of acapatamab, in combination with enzalutamide, abiraterone, or the PD-1 inhibitor AMG 404 in patients with earlier-line mCRPC. An ongoing open-label, Phase 1b study is evaluating the safety and tolerability of acapatamab in adults with relapsed/refractory NSCLC.

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.

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 any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd. or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) into our business (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), or the Five Prime Therapeutics, 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.

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. Further, any 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 for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

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