FDA Approves LUMAKRAS™ (Sotorasib), The First And Only Targeted Treatment For Patients With KRAS G12C-Mutated Locally Advanced Or Metastatic Non-Small Cell Lung Cancer

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KRAS G12C, a Driver Mutation Found in About 13% of Patients With Non-Squamous Non-Small Cell Lung Cancer, is Now Actionable(1)

Once-Daily Dosing of LUMAKRAS Demonstrated Durable Responses and a Positive Benefit-Risk Profile

Biomarker Testing Critical to Identify KRAS G12C Mutation

THOUSAND OAKS, Calif., May 28, 2021 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved LUMAKRAS ™(sotorasib) 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. LUMAKRAS has received 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).

To view the multimedia assets associated with this release, please click: https://www.multivu.com/players/English/8812853-amgen-fda-approval-lumakras-sotorasib-targeted-kras-g12c-lung-cancer/

"The FDA approval of LUMAKRAS is a breakthrough moment for patients with *KRAS* G12C-mutated non-small cell lung cancer because there is now a targeted therapy for this common, but previously elusive, mutation," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "*KRAS* has challenged cancer researchers for more than 40 years with many deeming it as 'undruggable.' The LUMAKRAS development program was a race against cancer for Amgen's scientists and clinical trial investigators who together have now successfully delivered this new medicine to patients in less than three years—from first patient dosed tdU.S. regulatory approval."

The FDA approval of LUMAKRAS is based on results from a subset of patients in CodeBreaK 100, the largest clinical trial conducted to date exclusively for patients with the *KRAS* G12C mutation. The trial demonstrated favorable efficacy and tolerability in 124 patients with *KRAS* G12C mutation-positive NSCLC who had disease progression after receiving an immunotherapy and/or chemotherapy. In the trial, 960 mg of LUMAKRAS administered orally once-daily demonstrated an ORR (a proportion of patients with ≥ 30% decrease in tumor) of 36% (95% CI: 28-45) with 81% (95% CI: 73-87) of patients achieving disease control (percentage of patients who have achieved complete response, partial response and stable disease for more than three months). The median DoR was 10 months. The most common adverse reactions (≥ 20%) were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity and cough. Adverse reactions resulting in permanent discontinuation of LUMAKRAS occurred in 9% of patients.

"Sotorasib represents a major advancement in oncology and changes the treatment paradigm for patients with *KRAS* G12C-mutated non-small cell lung cancer," said Bob T. Li, M.D., Ph.D., MPH, principal investigator at Memorial Sloan Kettering Cancer Center. "Patients with non-small cell lung cancer who have progressed beyond first-line treatment face a poor prognosis and have limited treatment options available to them. Sotorasib delivers a new option for these patients, and it is the first KRAS-targeted therapy to be approved after nearly four decades of research."

NSCLC accounts for approximately 84% of the 2.2 million new lung cancer diagnoses each year worldwide, including approximately 236,000 new cases in the U.S.[2,3] *KRAS* G12C is one of the most prevalent driver mutations in NSCLC, with about 13% of patients with non-squamous NSCLC in the U.S. having the *KRAS* G12C mutation.[1]

Amgen's Commitment to Comprehensive Biomarker Testing and Patient Support

About half of all patients with NSCLC harbor a targetable driver mutation, yet despite the integral role that biomarkers play in identifying patients who may benefit from targeted therapies, many patients are not tested.[4,5]

Amgen has partnered with two companies—Guardant Health and QIAGEN—to develop blood- and tissue-based companion diagnostics (CDx), respectively, for LUMAKRAS. With the addition of these tests, patients and clinicians will have more options and flexibility for conducting *KRAS* G12C biomarker testing.

"Biomarker testing for patients with non-small cell lung cancer is critical because it informs a patient's treatment path with a personalized and tailored approach. The only way to identify the *KRAS* G12C mutation is to test for it, so I urge patients to ask their care teams about comprehensive biomarker testing. It is important that patients and their healthcare providers know that *KRAS* G12C is now an actionable mutation," said Andrea Ferris, president and CEO of LUNGevity. "Today's FDA approval of a therapy targeted for *KRAS* G12C, one of the most prevalent biomarkers in non-small cell lung cancer, brings hope to the many patients who carry this mutation and is a significant moment for the lung cancer community who need more innovative treatment options."

Amgen is committed to supporting patients with NSCLC and to helping appropriate patients with affordable access to LUMAKRAS. Patients, caregivers and physicians who need support, tools or resources can contact Amgen Assist360™(1-888-4ASSIST)Amgen also provides patient assistance for its medicines marketed in the U.S. in a variety of ways, including free medicines through the Amgen Safety Net Foundation for qualifying individuals with no or limited drug coverage.

Amgen to Webcast Investor Call on LUMAKRAS FDA Approval

Amgen will host a webcast call for the investment community on Tuesday, June 1, 2021 at 5 a.m. PT / 8 a.m. ET. David M. Reese, M.D., executive vice president of Research and Development and Murdo Gordon, executive vice president of Global Commercial Operations at Amgen will participate to discuss the recent FDA approval of LUMAKRAS.

Live audio of the investor call 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 LUMAKRAS ™(sotorasib)

Amgen has taken on one of the toughest challenges of the last 40 years in cancer research by developing LUMAKRAS, a $KRAS^{G12C}$ inhibitor.[6] LUMAKRAS was the first $KRAS^{G12C}$ inhibitor to enter the clinic and is being studied in the largest clinical program exploring 11 combinations with global investigator sites spanning five continents.

LUMAKRAS has demonstrated a positive benefit-risk profile with rapid, deep and durable anticancer activity in patients with locally advanced and metastatic non-small cell lung cancer (NSCLC) harboring the *KRAS* G12C mutation with a once daily oral formulation. As part of the evaluation for this accelerated approval, FDA is requiring a post-marketing trial to investigate whether a lower dose will have a similar clinical effect.

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

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 submitted a Marketing Authorization Application (MAA) in the EU in December 2020 and New Drug Applications in Japan (J-NDA) and Switzerland in April 2021. Additionally, Amgen submitted MAAs for sotorasib in Australia, Brazil, Canada and the United Kingdom in January 2021 to participate in the FDA's Project Orbis initiative. Sotorasib was granted Breakthrough Therapy Designation in the U.S. and China.

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 ™in 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.[3] 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.[7]

KRAS G12C is the most common *KRAS* mutation in NSCLC.[8] In the U.S., about 13% of patients with non-squamous NSCLC harbor the *KRAS* G12C mutation.[1] 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.[9]

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 topline results are expected later in 2021.

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.

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

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 integration 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.

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