EUROPEAN COMMISSION APPROVES LUMYKRAS® (SOTORASIB) FOR PATIENTS WITH KRAS G12C-MUTATED ADVANCED NON-SMALL CELL LUNG CANCER

January 10, 2022

First Targeted Therapy for Patients With the KRAS G12C Mutation Approved in the European Union

Approval Based on Pivotal CodeBreaK 100 Data Demonstrating Durable Responses and a Favorable Benefit-Risk Profile With LUMYKRAS

LUMYKRAS Now Approved in 35 Countries Around the World Through Most Advanced KRAS G12C Clinical Development Program

THOUSAND OAKS, Calif., Jan. 9, 2022 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the European Commission (EC) has granted conditional marketing authorization for LUMYKRAS® (sotorasib), a first-in-class $KRAS^{G12C}$ inhibitor, for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with *KRAS* G12C mutation and who have progressed after at least one prior line of systemic therapy. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

"The approval of LUMYKRAS, the first and only targeted therapy for *KRAS* G12C-mutated NSCLC with proven efficacy, has the potential to transform treatment outcomes for people in the European Union living with this notoriously difficult-to-treat cancer," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Amgen's landmark scientific discovery allowed investigators to advance the first $KRAS^{G12C}$ inhibitor into the clinic, and we look forward to bringing this critical innovation to more patients across the globe."

The EC decision follows the recommendation for approval by the Committee for Medicinal Products for Human Use (CHMP) and is based on the positive results from the Phase 2 CodeBreaK 100 clinical trial in NSCLC, the largest trial conducted to date for patients with the *KRAS* G12C mutation. LUMYKRAS 960 mg, administered orally once-daily, demonstrated an objective response rate of 37.1% (95% CI: 28.6-46.2) and a median duration of response (DoR) of 11.1 months. The most common adverse reactions were diarrhea (34%), nausea (25%), and fatigue (21%). The most common severe (grade ≥ 3) adverse reactions were increased alanine aminotransferase level (ALT; 5%), increased aspartate aminotransferase (AST; 4%), and diarrhea (4%).

NSCLC accounts for approximately 84% of the 2.2 million new lung cancer diagnoses globally each year, including approximately 400,000 new cases in Europe [1,2] *KRAS* G12C is one of the most prevalent driver mutations in NSCLC, with about 13-15% of European patients with non-squamous NSCLC having the *KRAS* G12C mutation.[3,4] With EC approval, and subject to local reimbursement applications, clinicians in all European Union member countries, as well as Norway, Iceland, and Liechtenstein, will be able to offer LUMYKRAS to appropriate patients with NSCLC.

About LUMAKRAS®/LUMYKRAS® (sotorasib)

Amgen took on one of the toughest challenges of the last 40 years in cancer research by developing LUMAKRAS/LUMYKRAS, a $KRAS^{G12C}$ inhibitor.[5] LUMAKRAS/LUMYKRAS 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.[6]

Amgen is progressing the largest and broadest global $KRAS^{G12C}$ inhibitor development program with unparalleled speed and exploring more than 10 sotorasib combination regimens, including triplets, with clinical trial sites spanning five continents. To date, over 4,000 patients around the world have received LUMAKRAS/LUMYKRAS through the clinical development program and commercial use.

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.

Regulatory approvals have also been received in the United Arab Emirates (LUMAKRAS), Switzerland (LUMYKRAS), and under the FDA's Project Orbis in Canada (LUMAKRAS) and Great Britain (LUMYKRAS). Through Project Orbis, Amgen also has Marketing Authorization Applications (MAAs) for sotorasib in review in Australia, Brazil, Singapore and Israel. Additionally, Amgen has submitted MAAs in Japan, South Korea, Turkey, Taiwan, Colombia, Thailand, Mexico, Hong Kong, Saudi Arabia, Argentina, Kuwait and Qatar.

LUMAKRAS/LUMYKRAS is also being studied in multiple other solid tumors.[7]

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] About 13% of patients with non-squamous NSCLC harbor the *KRAS* G12C mutation.[4] 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.[11]

About CodeBreaK

The CodeBreaK clinical development program for Amgen's drug sotorasib is designed to study patients with an advanced solid tumor with the *KRAS* G12C mutation and address the longstanding unmet medical need for these cancers.

CodeBreaK 100, the Phase 1 and 2, first-in-human, open-label multicenter study, enrolled patients with *KRAS* G12C-mutant solid tumors.[11] 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.[7] The Phase 2 trial in colorectal cancer (CRC) is fully enrolled and results have been submitted for publication.[12]

CodeBreaK 200, the global Phase 3 randomized active-controlled study comparing sotorasib to docetaxel in *KRAS* G12C-mutated NSCLC completed enrollment of 345 patients. Eligible patients had previously treated, locally-advanced and unresectable or metastatic *KRAS* G12C-mutated NSCLC. The primary endpoint is progression-free survival and key secondary endpoints include overall survival, objective response rate, and patient-reported outcomes.

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.

Important EU/EEA Product Information

LUMYKRAS® (sotorasib) as monotherapy is indicated for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with *KRAS G12C* mutation and who have progressed after at least one prior line of systemic therapy.

Important EU/EEA Safety information

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Contraindications

LUMYKRAS is contraindicated in patients with a history of hypersensitivity to the active substance or to any of the excipients.

Special Warning and Precautions for Use

Hepatotoxicity: Sotorasib can cause hepatotoxicity, which may lead to drug-induced liver injury (DILI) and hepatitis. Sotorasib has been associated with transient elevations of serum transaminases (ALT and AST). These elevations improved or resolved with dose modification or permanent discontinuation of treatment and did not result in any cases of liver failure or fatal cases in clinical studies. Among patients who experienced hepatotoxicity, 38% had hepatotoxicity leading to dose interruption or dose reduction. Overall, 26% of patients with hepatotoxicity received concurrent corticosteroids. Cases of liver enzyme increase can be asymptomatic. Patients should be monitored for liver function (ALT, AST, and total bilirubin) prior to the start of LUMYKRAS, 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. Based on the severity of the laboratory abnormalities, treatment with LUMYKRAS must be stopped until recovered to ≤ grade 1 or to baseline grade, and the dose must either be modified or permanently discontinue treatment as recommended (see section 4.2).

Interstitial Lung Disease (ILD)/pneumonitis: ILD/pneumonitis occurred in patients treated with LUMYKRAS with prior exposure to immunotherapy or radiotherapy (see section 4.8). Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g. dyspnoea, cough, fever). Immediately withhold LUMYKRAS in patients with suspected ILD/pneumonitis and permanently discontinue LUMYKRAS if no other potential causes of ILD/pneumonitis are identified (see section 4.2).

Lactose intolerance: LUMYKRAS contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose–galactose malabsorption should not take this medicinal product.

Adverse Reactions

The most common adverse reactions were diarrhoea (34%), nausea (25%) and fatigue (21%). The most common severe adverse reactions were increased alanine aminotransferase (ALT) (5%), increased aspartate aminotransferase (AST) (4%), and diarrhoea (4%). The most common adverse reactions leading to permanent discontinuation of treatment were increased ALT (1%) and increased AST (1%) and drug-induced liver injury (1%). The most common adverse reactions leading to dose modification were increased ALT (6%), diarrhoea (6%), increased AST (6%), nausea (3%), increased blood alkaline phosphatase (3%) and vomiting (2%).

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 U.S. 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 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 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 the world's largest independent biotechnology company, 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.

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, 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. 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. We or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market. 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. 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, 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.

CONTACT: Amgen, Thousand Oaks
Megan Fox, 805-447-1423 (media)
Michael Strapazon, 805-313-5553 (media)
Arvind Sood, 805-447-1060 (investors)

---

[1] World Health Organization. 2020 Statistics. Available at: https://www.who.int/en/news-room/fact-sheets/detail/cancer. Accessed on October 12, 2021.

[2] van Meerbeeck JP, et al. *Transl Lung Cancer Res*. 2021;10:2407-2417.

[3] Nassar AH, et al. *N Engl J Med*. 2021; 384: 185-187.

[4] Sebastian M, et al. *Lung Cancer*. 2021; 154: 51-61.

[5] Canon J, et al. *Nature*. 2019; 575: 217–223.

[6] Skoulidis F, et al. *N Engl J Med.* 2021;384:2371-2381.

[7] Hong DS, et al. N Engl J Med. 2020;383:1207-1217.

[8] Sung H, et al. *CA Cancer J Clin*. 2021; 71:209-249.

[9] American Cancer Society. Lung Cancer Survival Rates. 2021. Available at: https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/survival-rates.html. Accessed on September 2021.

[10] Arbour KC, et al. *Clin Cancer Res*. 2018; 24:334-340.

[11] Spira Al, et al. *Lung Cancer*. 2021;159 :1-9.

[12] Fakih MG, et al. *Lancet Oncol.* 2022;23:115-124.

View original content to download multimedia:https://www.prnewswire.com/news-releases/european-commission-approves-lumykras-sotorasib-for-patients-with-kras-g12c-mutated-advanced-non-small-cell-lung-cancer-301456869.html

SOURCE Amgen