LUMYKRAS® (sotorasib) Receives Positive Opinion From EMA CHMP For Patients With KRAS G12C-Mutated Advanced Non-Small Cell Lung Cancer

November 12, 2021

First Targeted Therapy for the KRAS G12C Mutation Recommended for Approval in the European Union

Positive Opinion Based on Clinical Results Demonstrating Durable Responses and a Favorable Benefit-Risk Profile With LUMYKRAS

KRAS G12C Mutation Shown to be Present in Approximately 13-15% of Patients in Europe With NSCLC[1],[2]

THOUSAND OAKS, Calif., Nov. 12, 2021 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending conditional marketing authorization of LUMYKRAS® (sotorasib), known as LUMAKRAS® in the U.S., 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. If the European Commission follows the recommendation for approval, LUMYKRAS will be the first targeted therapy available in the European Union (EU) for the *KRAS* G12C mutation, one of the most prevalent biomarkers in NSCLC.

"After 40 years of cancer research to target the *KRAS* mutation, many in the scientific community believed that KRAS was 'undruggable' leaving patients with this mutation with limited treatment options," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "The LUMYKRAS development program was designed to bring this targeted therapy to patients with *KRAS* G12C-mutated non-small cell lung cancer as quickly as possible. The EMA CHMP positive opinion brings patients in the EU closer to this transformative therapy and highlights our commitment to improving patient outcomes in difficult-to-treat cancers."

The CHMP based its positive opinion on results from the Phase 2 CodeBreaK 100 clinical trial, the largest trial conducted to date exclusively for patients with the *KRAS* G12C mutation. CodeBreaK 100 enrolled 126 patients, 124 of whom had centrally evaluable lesions at baseline. In the trial, LUMYKRAS demonstrated favorable efficacy and tolerability in these 124 patients with *KRAS* G12C mutation-positive NSCLC who had disease progression after receiving an immunotherapy and/or chemotherapy. LUMYKRAS 960 mg, administered orally once-daily, demonstrated an objective response rate (a proportion of patients with ≥ 30% decrease in the sum of the longest diameter of the target lesions compared with baseline) of 37.1% (95% CI: 28.6-46.2) a median duration of response (DoR) of 11.1 months, disease control rate (DCR) of 80.6% and median overall survival (OS) of 12.5 months.[3]

The most common treatment-related adverse reactions were diarrhea (32%), nausea (19%), increase in aminotransferase level (ALT) and increase in the aspartate aminotransferase level (AST) (15% each). The most common severe (grade ≥ 3) treatment-related adverse reactions were increased alanine aminotransferase (ALT; 6%), increased aspartate aminotransferase (AST; 6%), and diarrhea (4%). Only 7% of patients discontinued treatment due to treatment-related adverse events.[3]

The detailed CodeBreaK 100 Phase 2 data in NSCLC were presented at the 2020 World Conference on Lung Cancer (WCLC) and published in the *New England Journal of Medicine (NEJM)*.

"Patients with *KRAS* G12C-mutated NSCLC face poor prognosis and usually do not respond to currently available treatments," said Prof. Fabrice Barlesi, general director of Gustave Roussy, Villejuif, France**.** "The introduction of sotorasib in the EU as a novel treatment option would be a welcome development as a potentially new standard of care for the tens of thousands of patients with NSCLC living with this common mutation."

"The rapid tumor shrinkage and durable responses observed in the large-scale CodeBreaK 100 clinical trial that support this positive opinion are impressive and demonstrate the potential benefit sotorasib can offer our patients who have the *KRAS* G12C mutation," said Prof. Jürgen Wolf, M.D., medical director, Center for Integrated Oncology, University Hospital of Cologne, Germany. "As we move closer to a potential EMA approval, it is critical that we continue to increase the implementation of biomarker testing so we can match the right patients who may benefit from this first-in-class targeted therapy as quickly as possible."

NSCLC accounts for approximately 84% of the 2.2 million new lung cancer diagnoses each year worldwide, including approximately 400,000 new cases in Europe.[4,5] *KRAS* G12C is one of the most prevalent driver mutations in NSCLC, with about 13-15% of patients with non-squamous NSCLC having the $KRAS^{G12C}$ mutation.[6,7] LUMYKRAS, which is administered orally in a tablet formulation, binds with the mutated *KRAS* G12C protein keeping the mutated protein in an inactive state, thus preventing it from switching to its favored active state that supports cancer cell growth. LUMYKRAS has been shown to irreversibly bind to the inactive *KRAS* G12C protein, permanently locking it in an inactive state, inhibiting oncogenic signaling and tumorigenesis.[3,8]

The CHMP's recommendation will now be reviewed by the European Commission, which has the authority to approve medicines for use throughout the European Union. A European Commission decision is expected by mid-January 2022.

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 ™), and under Project Orbis in Canada (LUMAKRAS ™) and Great Britain (LUMYKRAS®). In addition to our EMA MAA, there are 16 regulatory applications pending review around the world.

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.[8] 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.[9]

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, LUMAKRAS/LUMYKRAS has treated over 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 Marketing Authorization Applications (MAAs) for sotorasib in review in Australia and Brazil. Additionally, Amgen has submitted MAAs in the Japan, Switzerland, South Korea, Singapore, Israel, Turkey, Taiwan, Colombia, Thailand, Mexico, Hong Kong, Saudi Arabia, Argentina and Kuwait.

LUMAKRAS/LUMYKRAS is also being studied in multiple other solid tumors.[10]

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.[11] 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.[12]

KRAS G12C is the most common *KRAS* mutation in NSCLC.[13] 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.[14]

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.

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[3]. 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.

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 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., 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. 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.

CONTACT: Amgen, Thousand Oaks
Trish Rowland, 805-447-5631 (media)
Megan Fox, 805-447-1423 (media)
Arvind Sood, 805-447-1060 (investors)

---

[1] Biernacka A, et al. *Cancer Genetics*. 2016; S2210-7762(16): 30021-7

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

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

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

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

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

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

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

[9] LUMAKRAS™ (sotorasib) prescribing information, Amgen. 05/2021.

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

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

[12] 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.

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

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

View original content to download multimedia:https://www.prnewswire.com/news-releases/lumykras-sotorasib-receives-positive-opinion-from-ema-chmp-for-patients-with-kras-g12c-mutated-advanced-non-small-cell-lung-cancer-301422994.html

SOURCE Amgen