LUMAKRAS® (SOTORASIB) RECEIVES APPROVAL IN JAPAN FOR PATIENTS WITH KRAS G12C-MUTATED ADVANCED NON-SMALL CELL LUNG CANCER

January 20, 2022

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

LUMAKRAS is the Only KRAS G12C Inhibitor Approved Anywhere in the World

THOUSAND OAKS, Calif., Jan. 20, 2022 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that LUMAKRAS® (sotorasib) has been approved in Japan for the treatment of *KRAS* G12C-mutated positive, unresectable, advanced and/or recurrent non-small cell lung cancer (NSCLC) that has progressed after systemic anticancer therapy.

"Today's approval of LUMAKRAS as the first and only $KRAS^{G12C}$ inhibitor marks a paradigm shift in the treatment of patients with non-small cell lung cancer in Japan," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "In just over three years since the first patient was dosed in the pivotal CodeBreaK 100 trial, LUMAKRAS is now approved in nearly 40 countries, illustrating our commitment to accelerating transformative medicines for patients living with cancers that have yet to be fully addressed."

The approval by the Japan Ministry of Health, Labour and Welfare (MHLW) is based on 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. Based on the approved label in Japan, LUMAKRAS 960 mg, orally administered once-daily, demonstrated an objective response rate (ORR) of 37% (95% CI: 28.8-46.6) in 123 evaluable patients (including 10 Japanese patients* with a data cutoff date: Sept. 1, 2020). Adverse reactions were observed in 128 (67%) of 190 patients† (including 13 Japanese patients). The most common adverse reactions (incidence ≥ 5%) were diarrhea (28%), nausea, increased alanine aminotransferase (ALT) and increased aspartate aminotransferase (AST) (16% each), fatigue (11%), increased blood alkaline phosphatase (8%), vomiting (7%) and abdominal pain (5%).

Results from the Phase 2 CodeBreaK clinical trial in NSCLC were published in *The New England Journal of Medicine*.

"*KRAS* gene mutations are one of the oldest known cancer driver gene mutations," said Steve Sugino, president and representative director, Amgen K.K. "However, it has proven to be very difficult to develop drugs for the treatment of *KRAS* gene mutations. For nearly 40 years, researchers have said that the mutation was 'undruggable.' I am very pleased that LUMAKRAS is now approved as a new treatment option for patients in Japan."

"The prognosis for patients with non-small cell lung cancer who have distant metastases or whose disease has relapsed after surgery, is generally poor," said Tetsuya Mitsudomi, M.D., professor, Department of Surgery, Division of Thoracic Surgery at Kindai University School of Medicine, past-president of the International Association for the Study of Lung Cancer (IASLC) and past-president of the Japan Lung Cancer Society (JLCS). "Recent developments in molecular-targeted drugs and immunotherapy have dramatically improved the prognosis for these patients. However, despite the relatively high frequency of the *KRAS* G12C mutation, no drugs specifically targeting this mutation have been available until recently. Therefore, the approval of LUMAKRAS in Japan is a major milestone in the treatment of non-small cell lung cancer patients with *KRAS* G12C mutations."

On March 11, 2021, the MHLW designated sotorasib as an orphan drug.

*3 subjects (including 1 Japanese subject) without measurable lesions at baseline as determined by the central review were excluded.
†Patients with non-small cell lung cancer who received at least 1 dose of this drug 960 mg in the phase I and II parts.

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.[1] 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.[2]

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. LUMAKRAS/LUMYKRAS® is also approved in the United Arab Emirates, the European Union and Switzerland, and in Canada and Great Britain under the FDA's Project Orbis. 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 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.[3]

About Non-Small Cell Lung Cancer and the *KRAS* G12C Mutation
Lung cancer is the second most prevalent cancer in the world, and the total number of patients in Japan is estimated to be about 169,000.[4,5] Lung cancer is also the leading cause of cancer site-specific mortality worldwide and in Japan, with an estimated 82,300 deaths annually.[5] About 85-90% of lung cancer patients are classified as having NSCLC (such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma).[6] NSCLC is a life-threatening, serious disease, and the 5-year survival rate of patients with stage IV NSCLC in Japan is 10.8% for adenocarcinoma and 2.7% for

squamous cell carcinoma, indicating that the prognosis of this disease is still poor.[7]

KRAS G12C is the most common *KRAS* mutation in NSCLC.[8] *KRAS* G12C mutation is reported to be found in approximately 13% of lung adenocarcinoma in the U.S. and 4.5% of non-squamous cell carcinoma in Japan.[9,10] There is a significant unmet need as there are limited treatment options for patients with NSCLC harboring *KRAS* G12C mutations who have failed or lost response to first-line treatment. Outcomes with available therapies have been suboptimal, with median progression-free survival after second-line therapy reported to be approximately 4 months in patients with NSCLC harboring *KRAS* G12C mutations.[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.[2,3] 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.[2] The Phase 2 trial in colorectal cancer (CRC) is fully enrolled and results have been published.[11]

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 Japan Product information

Product Name:	LUMAKRAS® TABLETS 120 mg
Generic Name:	sotorasib
Indication:	*KRAS* G12C mutated, unresectable, advanced and/or recurrent non-small cell lung cancer that has progressed after systemic anticancer therapy
Precautions related to indications:	• The product should be administered to patients who are confirmed as *KRAS* G12C-mutated by a pathologist with adequate experience or by testing at a testing facility. Approved in vitro diagnostics should be used for the testing. List of the approved in vitro diagnostics is available on the following website. https://www.pmda.go.jp/review-services/drug-reviews/review-information/cd/0001.html • Physicians should select patients to be treated with the product based on their good understanding of the "17. Clinical Studies" section of the package insert, and of the efficacy and safety of the product, with careful consideration of the use of therapies other than the product. • The efficacy and safety of the product in the first-line therapy have not been established. • The efficacy and safety of the product in postoperative adjuvant therapy have not been established.
Dosage and Administration:	The usual adult dosage is 960 mg of sotorasib administered orally once daily. The dose may be reduced according to the patient's condition.

Please refer to the latest package insert for details.

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 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 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.

Amgen K.K.
Amgen K.K. is the Japanese subsidiary of Amgen Inc., the largest independent biotechnology company in the world. In October 2013, we began our business as Amgen Astellas BioPharma, a joint venture with Astellas Pharma. On April 1, 2020, we became a wholly owned subsidiary of Amgen and changed our trade name. Amgen K.K. focuses on areas with high unmet medical needs, including cardiovascular disease, cancer, bone disease, inflammatory/immunologic disease, and neurological disease. With our mission "To serve patients – everything we can do now" approximately 600 employees are engaged in everything from clinical development to marketing.

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., Generate Biomedicines, Inc., Arrakis Therapeutics, Inc., 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.

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