Amgen Announces New LUMAKRAS™ (sotorasib) Combination Data From Phase 1b CodeBreaK 101 Study In Patients With KRAS G12C-mutated Cancers At AACR-NCI-EORTC 2021

October 7, 2021

Broadest KRAS G12C Development Program Evaluating Multiple Combination Therapy Approaches

THOUSAND OAKS, Calif., Oct. 7, 2021 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced new combination study results from the Phase 1b CodeBreaK 101 study, a comprehensive global master protocol trial evaluating the safety and efficacy of LUMAKRAS™ (sotorasib), the first and only approved $KRAS^{G12C}$ inhibitor, in more than 10 different investigational combination regimens for the treatment of patients with *KRAS* G12C-mutated cancers. Results from two arms of the study — LUMAKRAS with afatinib, a pan-ErbB tyrosine kinase inhibitor, and LUMAKRAS with trametinib, a mitogen-activated protein kinase inhibitor (MEKi) — will be presented at the plenary session titled 'Drugging Difficult Targets' during the AACR-NCI-EORTC 2021 Virtual International Conference on Molecular Targets and Cancer Therapeutics on Saturday, Oct. 9, 2021.

"A critical component of cancer drug development is to interrogate multiple pathways to understand whether different combinations can meaningfully advance cancer care. For this reason, Amgen has undertaken the broadest and most comprehensive global clinical development program for patients with the *KRAS* G12C mutation, exploring multiple combinations that will allow us to understand where we can best serve patients," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Consistent with our master protocol clinical trial design, which allows us to rapidly add, expand or remove cohorts to quickly understand what combinations work best for patients, Amgen will take these afatinib and trametinib results into account as we prioritize which combinations to move forward within our comprehensive LUMAKRAS development program. We look forward to presenting additional data, including PD-1 and SHP2 combination datasets, in the coming months."

LUMAKRAS in Combination with Afatinib (Abstract LBA6581)
The LUMAKRAS and afatinib combination arm enrolled 33 heavily pre-treated patients with *KRAS* G12C-mutated non-small cell lung cancer (NSCLC), including five patients previously treated with LUMAKRAS monotherapy. Ten patients received 20 mg of afatinib/960 mg of sotorasib (cohort 1; 4 patients with prior LUMAKRAS experience) and 23 patients received 30 mg of afatinib/960 mg of sotorasib (cohort 2; 1 patient with prior LUMAKRAS experience). The objective response rate (ORR) was 20% in cohort 1 and 35% in cohort 2, and the disease control rate was 70% and 74% in the two cohorts, respectively.

The most common treatment-related adverse events (TRAEs) for this study were diarrhea, nausea, and vomiting. TRAEs of grade 3 occurred in 30% of patients in both dose groups with diarrhea being the most common.

LUMAKRAS in Combination with Trametinib (Abstract LBA6580)
In CodeBreaK 101, the combination of LUMAKRAS and trametinib showed antitumor activity in heavily pre-treated patients with *KRAS* G12C-mutated solid tumors, including those with prior $KRAS^{G12C}$ inhibitor treatment. A total of 41 patients were enrolled in the Phase 1b study with 18 patients with NSCLC, 18 patients with colorectal cancer (CRC) and five patients with other solid tumors. The maximum tolerated dose tested was 2 mg trametinib/960 mg sotorasib administered daily.

In patients with CRC who were $KRAS^{G12C}$ inhibitor naïve, 9% achieved partial response (1 of 11), and 82% achieved disease control (9 of 11). In patients who were previously treated with a $KRAS^{G12C}$ inhibitor, 14% achieved partial response (1 of 7), and 86% achieved disease control (6 of 7).

In patients with NSCLC who were $KRAS^{G12C}$ inhibitor naïve, 20% achieved partial response (3 of 15) and 87% achieved disease control (13 of 15). In patients who were previously treated with a $KRAS^{G12C}$ inhibitor, 67% achieved disease control (2 of 3).

The most common TRAEs for this study were diarrhea, rash, dermatitis acneiform, nausea and vomiting. No new safety concerns were identified.

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.[1] 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.[2]

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, and in Canada and Great Britain under Project Orbis.

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 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 an MAA in the European Union, Japan, Switzerland, South Korea, Singapore, Israel, Turkey, Taiwan, Colombia, Thailand, Mexico and Hong Kong.

LUMAKRAS is also being studied in multiple other solid tumors.[1]

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. 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.

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 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), 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.

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

References:

1. Hong DS, et al. *N Engl J Med.* 2020;383:1207-1217.
2. Skoulidis F, Li BT, Dy GK, et al. *N Engl J Med*. 2021;384(25):2371-2381. doi:10.1056/NEJMoa2103695.

View original content to download multimedia:https://www.prnewswire.com/news-releases/amgen-announces-new-lumakras-sotorasib-combination-data-from-phase-1b-codebreak-101-study-in-patients-with-kras-g12c-mutated-cancers-at-aacr-nci-eortc-2021-301394818.html

SOURCE Amgen