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MAJORITY WHIP

COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY
COMMITTEE ON APPROPRIATIONS
COMMITTEE ON THE JUDICIARY

United States Senate

WASHINGTON, DC 20510-1304

May 10, 2024

Mr. Robert Bradway
Chief Executive Officer
Amgen
One Amgen Center Drive
Thousand Oaks, CA 91320

Dear Mr. Bradway:

I write regarding Amgen's actions and marketing strategy related to its oncology product, Lumakras (sotorasib). Recently, Amgen has pursued a series of unconventional activities regarding the dosing of Lumakras that raises questions about whether the company is putting profits before patients, while diminishing concerns about harsh side effects.

Lumakras holds the potential to meaningfully improve outcomes for cancer patients with common gene mutations that previously have had few treatment options available. Amgen obtained accelerated approval from the Food and Drug Administration (FDA) for Lumakras in May 2021, with an indication for the treatment of non-small cell lung cancer, and launched with a list price of $17,900 per month.

However, FDA stated in its original review that it did not consider the proposed dosing regimen to be optimal. Thus, as one condition of FDA's accelerated approval, the agency directed Amgen to conduct a post-marketing study consisting of a randomized trial to compare the safety and efficacy of the proposed 960 mg daily dose versus a lower daily dose of 240 mg, and complete that trial by October 2022.

Amgen announced the results of that FDA-mandated post-marketing dosing study in October 2023, which showed that a lower dose of 240 mg demonstrated similar efficacy while significantly reducing toxicity and serious adverse events, as anticipated by FDA in its original review. Despite this evidence, in December 2023, Amgen stated it would maintain the 960 mg daily dose on its approved labeling.

The basis for Amgen's decision not to transition to the 240 mg daily dose recommended for study by FDA is unclear, considering that this dosing regimen was demonstrated to have a more favorable toxicity profile with comparable efficacy, especially in the primary endpoint and drug absorption data. And a study recently published in the *JTO Clinical and Research Reports* examined real-world data of lower doses of Lumakras among patients of the Veterans Health Administration, finding that dose reduction was associated with significantly improved progression-free survival and overall survival. Amgen already markets 120 mg tablets, making any labeling change relatively straightforward. And in November 2023, Amgen disclosed a

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clinical trial to study a new single tablet formulation, suggesting that Amgen agrees with the FDA's directive—and the outcome of its post-marketing study—about the optimal dose.

An apparent reason to maintain the 960 mg dosage would be to maximize Amgen's profits. Implementing the 240 mg dosage would result in patients taking only one-quarter of the number of pills, cutting Amgen's revenue by 75 percent. The decision not to pursue the reduced dosage comes at a significant cost to patients and American taxpayers, as evidenced by the $124 million cost of Lumakras to just the Medicare program in 2022 alone. This is in addition to the cost to patient health resulting from the increased toxicity of the 960 mg dosage—in which the FDA-mandated post-marketing study found a nearly double rate of serious or life-threatening adverse effects.

The FDA recently announced Project Optimus, a program to reform the dose selection paradigm in oncology drug development to correct for the historic preference of manufacturers pursuing the maximum tolerated dose, which can provide additional toxicity without added efficacy. FDA has noted that improving dose-finding to account for safety and tolerability—while maintaining efficacy—is in the best interest of patients. The *Consolidated Appropriations Act, 2023* (P.L. 117-328) carried report language in the explanatory statement directing FDA to support efforts to optimize oncology drug dosing, including through "frequency adjustments [to] reduce waste and/or toxicities of treatment without compromising efficacy."

I introduced the bipartisan *Interagency Patent Coordination and Improvement Act* (S. 79), which would establish a task force between the FDA and the U.S. Patent and Trademark Office to enhance information sharing between the two agencies to, among other activities, prevent gamesmanship and patent abuses that limit competition for prescription drugs. This legislation was reported out of the Senate Judiciary Committee favorably. I understand that Amgen added an additional patent covering Lumakras in the FDA's Orange Book in December 2023, providing patent protection until 2040, and recently filed another patent application regarding Lumakras' dosing regimen.

As someone who lost his father to lung cancer, I believe wholeheartedly that cancer patients deserve access to safe, effective medications to reduce suffering, improve quality of life, and extend years of life. For that reason, I have spent years advocating for funding increases to the National Institutes of Health, to enhance our investments in medical breakthroughs for patients. But patients also deserve affordable medications that do not force them to choose between their medications, rent, or groceries. And if there is an opportunity to reduce side effects and toxicities that can harm quality of life, every reasonable action should be pursued.

To provide clarity on Amgen's actions and whether a labeled daily dose of 240 mg or 960 mg is superior, I request a written explanation of Amgen's dosing, research, and marketing strategy for Lumakras by June 10, 2024. Specifically, I request that you answer the following questions:

1. Has FDA requested that Amgen change its labeling to lower the dose to 240 mg? Please provide all copies of communications between Amgen and FDA on this subject.

2. Does Amgen believe that a daily dose of 960 mg is the proper and optimized starting dose for patients, as compared to 240 mg? If so, please explain why Amgen has filed patent applications claiming an effective method of treating cancer with lower doses.

3. Does Amgen intend to withdraw its current drug dosage formulations if it obtains regulatory approval of a new 240 mg formulation?

4. If the recommended dosage in the labeling is lowered to 240 mg, does Amgen commit to not increase the per-milligram cost of the drug?

Thank you for your attention to this matter. I look forward to your response.

Sincerely,

Richard J. Durbin
United States Senator