



Tezepelumab Granted Priority Review By U.S. FDA

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Tezepelumab is the First and Only Biologic to Consistently and Significantly Reduce Asthma Exacerbations in a Broad Population of Patients Across Phase 2 and 3 Clinical Trials

THOUSAND OAKS, Calif., July 7, 2021 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has accepted a Biologics License Application (BLA) and granted Priority Review for tezepelumab in the treatment of asthma. Tezepelumab is being developed by Amgen in collaboration with AstraZeneca.

The FDA grants Priority Review to applications for medicines that offer significant advantages over available options by demonstrating safety or efficacy improvements, preventing serious conditions or enhancing patient compliance.¹ The Prescription Drug User Fee Act goal date for a decision by the FDA is during the first quarter of 2022.

Despite recent advances in severe asthma, many patients may not qualify for or respond well to current biologic medicines.²⁻⁵ Patients with severe, uncontrolled asthma experience frequent exacerbations, significant limitations on lung function and a reduced quality of life.^{2,6,7}

"Severe asthma is a challenging, complex disease for physicians and millions of patients and has a high unmet medical need," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "We are proud to advance an innovative, first-in-class monoclonal antibody that targets the top of the inflammatory cascade and represents a potentially transformative treatment option for a broad population of patients with severe asthma. We look forward to bringing tezepelumab to patients as quickly as possible."

The BLA was based on results from the PATHFINDER clinical trial program, including results from the pivotal NAVIGATOR Phase 3 trial in which tezepelumab demonstrated superiority across every primary and key secondary endpoint compared to placebo in a broad population of patients with uncontrolled asthma while receiving treatment with medium- or high-dose inhaled corticosteroids (ICS) plus at least one additional controller medication with or without oral corticosteroids (OCS).⁸ There were no clinically meaningful differences in safety results between the tezepelumab and placebo groups in the NAVIGATOR trial.⁸ The most frequently reported adverse events with tezepelumab were nasopharyngitis, upper respiratory tract infection and headache.⁸

Results from the NAVIGATOR Phase 3 trial were published in the [New England Journal of Medicine](#) in May 2021.

Tezepelumab was granted an FDA [Breakthrough Therapy Designation](#) for patients with severe asthma without an eosinophilic phenotype in September 2018.

About Severe Asthma

Globally, there are approximately 2.5 million patients with severe asthma who are uncontrolled or biologic eligible, with approximately 1 million in the U.S. Many patients with severe asthma have an inadequate response to currently available biologics and oral corticosteroids and thus fail to achieve asthma control.^{2,6,9} Uncontrolled asthma occurs when symptoms persist despite treatment. Severe, uncontrolled asthma is debilitating with patients experiencing frequent exacerbations, significant limitations on lung function and a reduced quality of life.^{2,6,9} Patients with severe uncontrolled asthma have twice the risk of asthma-related hospitalizations.^{10,11} There is also a significant socio-economic burden, with these severe, uncontrolled asthma patients accounting for 50% of asthma-related costs.¹²

Multiple inflammatory pathways are involved in the pathogenesis of asthma.¹³⁻¹⁵ Eosinophilic asthma, and more broadly, T2 inflammation-driven asthma, accounts for about two-thirds of patients with severe asthma.¹⁵ These patients are typically characterized as having elevated levels of inflammatory biomarkers, including blood eosinophils, serum IgE and fractional exhaled nitric oxide (FeNO).^{16,17} However, many patients do not fit the criteria for eosinophilic or allergic asthma, may have unclear or multiple drivers of inflammation and may not qualify for or respond well to a current biologic medicine.¹⁷

About the NAVIGATOR and the PATHFINDER Clinical Trial Program

Building on the Phase 2b PATHWAY trial, the Phase 3 PATHFINDER program included two trials, NAVIGATOR^{8,18} and SOURCE.^{19,20} The program includes additional planned mechanistic and long-term safety trials.²¹

NAVIGATOR is a Phase 3, randomized, double-blinded, placebo-controlled trial in 1,061 adults (18–80 years old) and adolescents (12–17 years old) with severe, uncontrolled asthma, who were receiving treatment with medium- or high-dose inhaled corticosteroids (ICS) plus at least one additional controller medication with or without OCS. NAVIGATOR met the primary endpoint with tezepelumab added to standard of care (SoC) demonstrating a statistically significant and clinically meaningful reduction in the annualized asthma exacerbation rate (AAER) over 52 weeks in the overall patient population, compared to placebo added to SoC. The trial also met the primary endpoint in the subgroup of patients with baseline eosinophil counts less than 300 cells per microliter, with tezepelumab demonstrating a statistically significant and clinically meaningful reduction in AAER in that patient population. Similar reductions in AAER were observed in the subgroup of patients with baseline eosinophil counts less than 150 cells per microliter.^{21,22}

NAVIGATOR primary endpoints ⁸				
Endpoint	Timepoint	Annual Exacerbation Rate		Results <i>Tezepelumab added to SoC vs placebo added to SoC</i>
		Tezepelumab	Placebo	

AAER – overall patient population	Over 52 weeks	0.93 (95% CI: 0.80, 1.07)	2.10 (95% CI: 1.84, 2.39)	56% reduction (95% CI: 47, 63; p<0.001)
AAER – baseline eosinophil counts < 300 cells/ μ L	Over 52 weeks	1.02 (95% CI: 0.84, 1.23)	1.73 (95% CI: 1.46, 2.05)	41% reduction (95% CI: 25, 54; p<0.001)

CI: confidence interval

NAVIGATOR is the first Phase 3 trial to show benefit in severe asthma irrespective of eosinophils by targeting the thymic stromal lymphopoietin (TSLP). The [U.S. Food and Drug Administration Breakthrough Therapy Designation](#) was granted to tezepelumab in September 2018 for patients with severe asthma, without an eosinophilic phenotype.

SOURCE is a Phase 3 multicenter, randomized, double-blinded, parallel-group, placebo-controlled trial for 48 weeks in adult patients with severe asthma who require continuous treatment with ICS plus long-acting beta2-agonists (LABA), and chronic treatment with maintenance OCS therapy. In the trial, patients were randomized to receive tezepelumab 210 mg every four weeks or placebo as add-on therapy, with patients maintained on their currently prescribed ICS plus LABA, with or without other asthma controller therapy.

Patients who participated in the NAVIGATOR and SOURCE trials were eligible to continue in DESTINATION, a Phase 3 extension trial assessing long-term safety and efficacy.²³

About Tezepelumab

Tezepelumab is being developed by AstraZeneca in collaboration with Amgen (see AstraZeneca and Amgen collaboration below) as an investigational, potential first-in-class human monoclonal antibody that works on the primary source of inflammation: the airway epithelium, which is the first point of contact for viruses, allergens, pollutants and other environmental insults. Specifically, tezepelumab targets and blocks thymic stromal lymphopoietin (TSLP), a key epithelial cytokine that sits at the top of multiple inflammatory cascades and initiates an overreactive immune response to allergic, eosinophilic and other types of airway inflammation associated with severe asthma.^{24,25}

TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles.^{24,25} Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity.^{24,26} Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control.^{24,26} By working at the top of the cascade, tezepelumab helps stop inflammation at the source and has the potential to treat a broad population of severe asthma patients.^{24,26}

About the Amgen and AstraZeneca Collaboration

In 2020, Amgen and AstraZeneca updated the 2012 collaboration agreement for tezepelumab. Both companies will continue to share costs and profits equally after payment by AstraZeneca of a mid-single-digit royalty to Amgen. AstraZeneca continues to lead development and Amgen continues to lead manufacturing. All aspects of the collaboration are under the oversight of joint governing bodies. Under the amended agreement in North America, Amgen and AstraZeneca will jointly commercialize tezepelumab; Amgen will record sales in the U.S. and AstraZeneca will record sales in Canada. Outside the U.S., Amgen will record sales as collaboration revenue.

Amgen Inflammation

Amgen brings therapies to millions of people with inflammatory diseases, with a focus on serving unmet patient needs. For those with debilitating moderate to severe rheumatoid arthritis, psoriatic arthritis, moderate to severe plaque psoriasis, ankylosing spondylitis, asthma, and other chronic conditions, the suffering and needs are severe. Complex diseases of inflammation have defied simple solutions, and the breadth of inflammatory disease and the burden patients bear is not well understood.

For more than two decades, Amgen has been committed to advancing the science and the understanding around inflammation to address the unmet patient needs that exist and expanding our portfolio. We lead with science through discovery research that is disease-agnostic and biology-first, modality-second. In doing so, we have introduced and evolved novel therapies that have changed the lives of patients.

Our commitment to patients is reflected not only in where we have succeeded, but in where we have failed and opened new doors. Throughout, we have remained dedicated to the principle of leading with science, pursuing where pathways and promising discoveries in inflammation take us, and not relenting until innovative solutions for patients are found. It's a commitment that extends beyond introducing novel therapies. We are focused on improving the entire patient journey.

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.

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. 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 Amgen's 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 its 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 Amgen projects. 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 Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints Amgen has selected. Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with its products, including its devices, after they are on the market.

Amgen's results may be affected by its 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 its products and global economic conditions. In addition, sales of Amgen's 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, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain of its 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 Amgen's manufacturing activities, the distribution of Amgen's products, the commercialization of Amgen's product candidates, and Amgen's clinical trial operations, and any such events may have a material adverse effect on Amgen's product development, product sales, business and results of operations. Amgen relies on collaborations with third parties for the development of some of its product candidates and for the commercialization and sales of some of its commercial products. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. Certain of Amgen's distributors, customers and payers have substantial purchasing leverage in their dealings with Amgen. The discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on its business and results of operations. Amgen's 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 Amgen has acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of Amgen's systems and Amgen's data. Amgen's stock price may be volatile and may be affected by a number of events. Global economic conditions may magnify certain risks that affect our business. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all.

The scientific information discussed in this news release related to Amgen's 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 Amgen's 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.

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