New Tezepelumab Data Continue To Strengthen Profile For A Broad Population Of Severe Asthma Patients

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NAVIGATOR Data Published in New England Journal of Medicine, and Latest Data from Tezepelumab Clinical Program Presented at ATS 2021 International Conference

Tezepelumab Reduced Exacerbations by 77% in Subgroup of Patients with Elevated Inflammatory Biomarkers in NAVIGATOR

Tezepelumab Reduced Exacerbations Requiring Hospitalization by 85%

THOUSAND OAKS, Calif., May 13, 2021 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca today announced detailed results for tezepelumab, a potential first-in-class treatment, from the pivotal NAVIGATOR Phase 3 trial demonstrating superiority across every primary and key secondary endpoint in a broad population of severe asthma patients, compared to placebo when added to standard of care (SoC). These results were published in the *New England Journal of Medicine* and will be presented this week at the American Thoracic Society (ATS) 2021 International Conference.[1,2]

In one of the pre-specified exploratory analyses of NAVIGATOR, reductions in annualized asthma exacerbation rates (AAERs) were observed over 52 weeks in tezepelumab-treated patients compared to placebo when added to SoC across four patient subgroups, based on blood eosinophil count and fractional exhaled nitric oxide (FeNO) levels. Blood eosinophil counts and FeNO levels are two key inflammatory biomarkers used by clinicians to inform treatment options and were defined as blood eosinophil count (≥300 or <300 cells per microlitre) and FeNO (≥25 or <25 parts per billion).

In patients with elevated baseline blood eosinophil counts (≥300 cells per microlitre) and FeNO levels (≥25 parts per billion), tezepelumab achieved a clinically meaningful 77% reduction in the AAER, compared to placebo.[1,2]

In a separate exploratory analysis of exacerbations requiring hospitalizations, tezepelumab showed an 85% reduction over 52 weeks compared to placebo when added to SoC.

Tezepelumab also demonstrated statistically significant improvements in key secondary endpoints compared to placebo in lung function, asthma control and health-related quality of life. Improvements were observed in tezepelumab-treated patients as early as week two of treatment or the first time point assessment and were sustained throughout the treatment period.[1]

These results build on the NAVIGATOR data presented in February 2021 which showed a statistically significant and clinically meaningful[3] reduction in the primary endpoint of AAER over 52 weeks in the overall patient population. Clinically meaningful reductions in AAER compared to placebo were observed in the tezepelumab-treated patients irrespective of blood eosinophil counts, allergy status or FeNO level.[1]

"Managing severe asthma is challenging with multiple inflammatory pathways often contributing to the complexity of a patient's disease. These latest results underscore the potential of tezepelumab to transform treatment for a broad population of severe asthma patients regardless of their type of inflammation," said Professor Andrew Menzies-Gow, Director of the Lung Division, Royal Brompton Hospital, London, UK, and principal investigator of the NAVIGATOR Phase 3 trial.

"Severe, uncontrolled asthma is debilitating, with patients experiencing frequent exacerbations that lead to hospitalization. For this reason, we were incredibly pleased to see that patients who received tezepelumab during the trial had a reduction in both ER visits and hospitalizations," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Advancing the science to address unmet patient needs such as these has been the driving force behind Amgen's inflammation research for more than two decades. Along with our partner AstraZeneca, we are incredibly proud of these results and tezepelumab's potential for a broad population of patients with asthma."

Additional Data to be Presented

Further results from the tezepelumab PATHFINDER clinical trial program will be presented at the ATS conference this week, including the primary analyses from the SOURCE Phase 3 and CASCADE Phase 2 trials.

As previously disclosed, the SOURCE Phase 3 trial did not meet the primary endpoint of a statistically significant reduction in the daily oral corticosteroid (OCS) dose, without loss of asthma control, with tezepelumab compared to placebo. Data to be presented show the number of patients that achieved a ≥90% reduction in OCS dose was numerically higher for tezepelumab-treated patients at 54.1% compared to 46.1% in the placebo group.[4]

In SOURCE, tezepelumab-treated patients showed improvements in exacerbations, forced expiratory volume in one second and patient-reported outcomes compared to placebo,[4] consistent with improvements shown in pooled post-hoc analyses in OCS dependent patients from the PATHWAY Phase 2 and NAVIGATOR Phase 3 trials. New trials are being planned to evaluate the ability of tezepelumab to reduce OCS use while maintaining asthma control in patients with chronic maintenance OCS therapy. Any new trial would aim to address unique aspects of the SOURCE trial design that may have contributed to the result of the primary endpoint.

Also being presented at the ATS Conference, results from the CASCADE Phase 2 mechanistic trial showed that in a broad population of patients with moderate to severe asthma, tezepelumab reduced eosinophils in airway tissue compared to placebo across subgroups of baseline blood eosinophil count, FeNO level and allergic status.[5] Importantly, tezepelumab was also associated with a reduction in airway hyper-responsiveness compared to placebo,[5] which is a major hallmark of asthma irrespective of eosinophilic airway inflammation.

There were no clinically meaningful differences in safety results between the tezepelumab and placebo groups in NAVIGATOR,[1] SOURCE[4] and

CASCADE.[5] The most frequently reported adverse events for tezepelumab in the NAVIGATOR trial were nasopharyngitis, upper respiratory tract infection, headache and asthma,[1] in the SOURCE trial were nasopharyngitis, upper respiratory tract infection, asthma, and bronchitis bacterial, and in the CASCADE trial were nasopharyngitis, post-procedural (bronchoscopy) complications and headache.

About Severe Asthma

Globally, there are approximately 2.5 million severe asthma patients who are uncontrolled or biologic eligible, with approximately 1 million in the U.S. Many severe asthma patients have an inadequate response to currently available biologics and oral corticosteroids and thus fail to achieve asthma control.[6-8] 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.[6-8] Patients with severe uncontrolled asthma have twice the risk of asthma-related hospitalizations.[9,10] There is also a significant socio-economic burden, with these severe uncontrolled asthma patients accounting for 50% of asthma-related costs.[11]

Multiple inflammatory pathways are involved in the pathogenesis of asthma.[12-14] Eosinophilic asthma, and more broadly, T2 inflammation-driven asthma, accounts for about two-thirds of patients with severe asthma.[14] These patients are typically characterized as having elevated levels of inflammatory biomarkers, including blood eosinophils, serum IgE and fractional exhaled nitric oxide (FeNO).[15,16] 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.[16]

NAVIGATOR and the PATHFINDER Clinical Trial Program

Building on the Phase 2b PATHWAY trial, the Phase 3 PATHFINDER program included two trials, NAVIGATOR[1,17] and SOURCE.[4,18] The program includes an additional planned long-term safety trial, DESTINATION and a mechanistic trial, CASCADE.[5]

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 SoC demonstrating a statistically significant and clinically meaningful reduction in the 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 pstoper microliter.[25]

NAVIGATOR endpoint: AAER in patients grouped by baseline blood eosinophil count and FeNO[1]	
Biomarker subgroup	**Results over 52 weeks** *Tezepelumab added to SoC versus placebo added to SoC*
Blood eosinophil count ≥300 cells/mcl FeNO ≥25 parts per billion	77% reduction (95% CI: 67, 84)
Blood eosinophil count ≥300 cells/mcl FeNO <25 parts per billion	39% reduction (95% CI: -7, 65)
Blood eosinophil count <300 cells/mcl FeNO ≥25 parts per billion	53% reduction (95% CI: 33, 67)
Blood eosinophil count <300 cells/mcl FeNO <25 parts per billion	29% reduction (95% CI: 0, 50)

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.

CASCADE is a Phase 2 mechanistic, multicenter, randomized, double-blind, placebo-controlled, parallel-group trial in adults aged 18–75 years with moderate to severe, uncontrolled asthma. The primary endpoint was the change from baseline (pre-dose) to end of treatment in airway submucosal inflammatory cells (eosinophils, neutrophils, T cells and mast cells) from bronchoscopic biopsies.[5]

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.[19]

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.[20,21]

TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles.[20,21] Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity.[20,22] Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control.[20,22] 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.[20,22]

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, or the Otezla® (apremilast) acquisition (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), 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.

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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.

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