Tezepelumab NAVIGATOR Phase 3 Trial Met Primary Endpoint Of A Statistically Significant And Clinically Meaningful Reduction In Exacerbations In A Broad Population Of Patients With Severe Asthma

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Trial Also Met the Primary Endpoint in Patients With Low Levels of Eosinophils

THOUSAND OAKS, Calif., Nov. 9, 2020 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca today announced positive topline results from the Phase 3 NAVIGATOR trial in which the investigational medicine tezepelumab demonstrated a statistically significant reduction in exacerbations compared to placebo in patients with severe asthma.

The NAVIGATOR trial met the primary endpoint with tezepelumab added to standard of care (SoC) demonstrating a statistically significant and clinically meaningful reduction compared to placebo plus SoC in the annualized asthma exacerbation rate (AAER) over 52 weeks in the overall patient population. SoC was medium- or high-dose inhaled corticosteroids (ICS) plus at least one additional controller medication with or without oral corticosteroids (OCS).

In the subgroup of patients with baseline eosinophil counts less than 300 cells per microliter, the trial met the primary endpoint with tezepelumab demonstrating a statistically significant and clinically meaningful reduction in AAER. Similar reductions in AAER were observed in the subgroup of patients with baseline eosinophil counts less than 150 cells per microliter.

The significant exacerbation rate reductions demonstrated with tezepelumab in patients with baseline eosinophil counts less than 300 cells per microliter support the U.S. Food and Drug Administration Breakthrough Therapy Designation granted to tezepelumab in Sept. 2018 for patients with severe asthma, without an eosinophilic phenotype.

Tezepelumab was very well tolerated in patients with severe asthma. Preliminary analyses show no clinically meaningful differences in safety results between the tezepelumab and placebo groups. Results from the NAVIGATOR trial will be presented at an upcoming medical meeting.

Tezepelumab is a potential first-in-class medicine that blocks the action of thymic stromal lymphopoietin (TSLP), an epithelial cytokine that plays a key role across the spectrum of asthma inflammation.[1,2] NAVIGATOR is the first Phase 3 trial to show benefit in severe asthma by targeting TSLP.

"We are absolutely thrilled with the topline results of the NAVIGATOR study in this broad population of patients with severe asthma, regardless of eosinophil count," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Tezepelumab represents a potential new class of biologics that could enable us to treat severe asthma at the top of the inflammatory cascade, addressing a high unmet need among the millions of patients living with severe asthma throughout the world. Tezepelumab has the potential to revolutionize care with efficacy demonstrated even in patients with a low eosinophil count."

Professor Andrew Menzies-Gow, director of the Lung Division, Royal Brompton Hospital, London, UK, and principal investigator of the NAVIGATOR trial said: "Due to the complex nature of severe asthma, many patients continue to face debilitating asthma despite receiving standard of care inhaled medicines and currently approved biologics. Today's ground-breaking results show that tezepelumab has the potential to transform care for a broad population of severe asthma patients who are underserved today, including those without an eosinophilic phenotype."

Amgen and AstraZeneca Collaboration

Earlier 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.

About Tezepelumab

Tezepelumab is 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 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.[1,2,3]

TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles.[1,2] Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity.[2,3] Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control.[2,3] 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.[2,3]

NAVIGATOR and the PATHFINDER clinical trial program

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

NAVIGATOR is a Phase 3, randomized, double-blinded, placebo-controlled trial in adults (18–80 years old) and adolescents (12–17 years old) with severe, uncontrolled asthma, who were receiving treatment with medium- or high-dose ICS plus at least one additional controller medication with or without OCS. The trial population included approximately equal proportions of patients with high (≥ 300 cells/μL) and low (< 300 cells/μL) blood eosinophil counts. The trial comprised a five to six week screening period, a 52-week treatment period and a 12-week post-treatment follow-up period.

All patients received their prescribed controller medications without change throughout the trial.[4]

The primary efficacy endpoint was the annualized asthma exacerbation rate during the 52-week treatment period. Key secondary endpoints included the effect of tezepelumab on lung function, asthma control and health-related quality of life.[4]

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. The primary endpoint is the categorized % reduction from baseline in the daily OCS dose while not losing asthma control.[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.[5]

About Severe Asthma

Asthma is a complex and heterogeneous disease affecting an estimated 339 million people worldwide.[6,7] Approximately 10% of asthma patients have severe asthma.[6,7] Yet, many severe asthma patients have an inadequate response to currently available biologics and oral corticosteroids and thus fail to achieve asthma control.[6-8] 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 asthma account for twice as many asthma-related hospitalizations.[9,10] There is also a significant socio-economic burden, with these patients accounting for 50% of asthma-related costs.[11]

Multiple inflammatory pathways are involved in the pathogenesis of asthma.[12,13,14] 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).[4,15] 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.[15]

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 or potential collaboration in pursuit of therapeutic antibodies against COVID-19 (including statements regarding such collaboration's, or Amgen's, ability to discover and develop fully-human neutralizing antibodies targeting SARS-CoV-2 or antibodies against targets other than the SARS-CoV-2 receptor binding domain, and/or to produce any such antibodies to potentially prevent or treat 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.

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. 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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[1] Varricchi G, Pecoraro A, Marone G, *et al*. Thymic Stromal Lymphopoietin Isoforms, Inflammatory Disorders, and Cancer. *Front Immunol*. 2018; 9: 1595.

[2] Corren J, Parnes JR, Wang L, *et al.* Tezepelumab in Adults with Uncontrolled Asthma [published correction appears in *N Engl J Med*. 2019 May 23;380(21):2082]. *N Engl J Med.* 2017; 377 (10): 936-946.

[3] Roseti S, Corren J, Parnes JR, *et al*. Efficacy and safety of tezepelumab in adults with severe asthma: A randomized phase 2 study. European Respiratory Journal 2017; 50: OA3189.

[4] Clinicaltrials.gov. Study to Evaluate the Efficacy and Safety of Tezepelumab in Reducing Oral Corticosteroid Use in Adults With Oral Corticosteroid Dependent Asthma (SOURCE) [Online]. Available at: https://clinicaltrials.gov/ct2/show/NCT03406078. [Last accessed: September 2020].

[5] Clinicaltrials.gov. Extension Study to Evaluate the Safety and Tolerability of Tezepelumab in Adults and Adolescents With Severe, Uncontrolled Asthma (DESTINATION) [Online]. Available at: https://clinicaltrials.gov/ct2/show/NCT03706079. [Last accessed: September 2020].

[6] Kupczyk M, Wenzel S. U.S. and European severe asthma cohorts: what can they teach us about severe asthma? *J Intern Med* 2012;272:121–32.

[7] Wenzel S. Severe Asthma in Adults. *Am J Respir Crit Care Med*. 2005; 172; 149–60.

[8] Chung KF, Wenzel SE, Brozek JL, *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–73.

[9] Price D, Fletcher M, van der Molen T. Asthma control and management in 8,000 European patients: the Recognise Asthma and Link to Symptoms

and Experience (REALISE) survey. *NPJ Prim Care Respir Med* 2014; 12; 24: 14009.

[10] World Allergy Organization (WAO). The management of severe asthma: economic analysis of the cost of treatments for severe asthma. Available from: https://www.worldallergy.org/educational_programs/world_allergy_forum/anaheim2005/blaiss.php [Last accessed: September 2020]

[11] Busse WW. Biological Treatments for Severe Asthma: A Major Advance in Asthma Care. Allergol Int 2019; 68: 158–66.

[12] Godar M, Blanchetot C, de Haard H, *et al*. Personalized medicine with biologics for severe type 2 asthma: current status and future prospects. *MAbs*. 2018; 10 (1): 34–45.

[13] Rabe KF, Busse W, Pavord I, Castro M. Raising the clinical bar beyond current biologics in uncontrolled persistent asthma: translating emerging data in future clinical decisions. *EMJ Allergy Immunol*. 2018; 3: 60-9.

[14] Peters MC, Mekonnen ZK, Yuan S, *et al*. Measures of gene expression in sputum cells can identify TH2-high and TH2-low subtypes of asthma. *J Allergy Clin Immunol*. 2014; 133: 388–94.

[15] Fahy JV. Type 2 inflammation in asthma--present in most, absent in many. *Nat Rev Immunol*. 2015; 15: 57-65.

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