Tezepelumab Granted Breakthrough Therapy Designation By US FDA For The Treatment Of Patients With Severe Asthma Without An Eosinophilic Phenotype

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Designation Supported by Phase 2b PATHWAY Data That Demonstrated Tezepelumab Significantly Reduced Asthma Exacerbations Compared to Placebo in Severe Asthma Patients

THOUSAND OAKS, Calif., Sept. 6, 2018 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and AstraZeneca (NYSE: AZN) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for tezepelumab in patients with severe asthma without an eosinophilic phenotype.

A Breakthrough Therapy Designation is designed to expedite the development and regulatory review of medicines that are intended to treat a serious condition and that have shown encouraging early clinical results which may demonstrate substantial improvement on a clinically-significant endpoint over available medicines.

The Breakthrough Therapy Designation is supported by the tezepelumab Phase 2b PATHWAY data. The trial showed a significant reduction in the annual asthma exacerbation rate compared with placebo in a broad population of severe asthma patients independent of baseline blood eosinophil count or other type 2 (T2) inflammatory biomarkers. Currently available biologic therapies only target T2 driven inflammation. Tezepelumab is a potential first-in-class new medicine that blocks thymic stromal lymphopoietin (TSLP) – an upstream modulator of multiple inflammatory pathways.

"The Phase 2b PATHWAY trial data demonstrated tezepelumab's promise as a novel therapeutic option for a broad population of patients with severe asthma, including those ineligible for currently approved biologic therapies," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "The Breakthrough Designation will give us the opportunity to work closely with the FDA to bring tezepelumab to patients as quickly as possible."

Tezepelumab is currently in development in the Phase 3 PATHFINDER clinical trial program.

About Severe Asthma

Asthma affects 334 million people worldwide[1], and up to 10 percent of asthma patients have severe asthma, which may be uncontrolled despite high doses of standard-of-care asthma controller medicines and can require the use of chronic oral corticosteroids (OCS).[2-4] Severe uncontrolled asthma is debilitating with patients experiencing frequent exacerbations and significant limitations on lung function.[5,6]

Multiple inflammatory pathways are involved in the pathogenesis of asthma.[7] T2 inflammation-driven asthma, which includes eosinophilic phenotype, is present in over two-thirds of patients with severe asthma and is typically characterized by elevated levels of T2 inflammatory biomarkers, including blood eosinophils, serum IgE and fractional exhaled nitric oxide (FeNO).[8,9] Conversely, approximately one-third of patients with severe asthma do not present with increased T2 inflammation.[10]

About Tezepelumab

Tezepelumab is a potential first-in-class medicine blocking TSLP, an epithelial cytokine, critical in the initiation and persistence of airway inflammation. Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells resulting in the prevention of asthma exacerbations and improved asthma control. Due to its activity early in the inflammation cascade, tezepelumab may be suitable for a broad population of patients with severe, uncontrolled asthma irrespective of patient phenotype or T2 biomarker status. Tezepelumab is being developed by AstraZeneca in collaboration with Amgen.

About the PATHWAY Phase 2b Trial

The PATHWAY Phase 2b data were published in the *New England Journal of Medicine* and presented at the European Respiratory Society International Congress in September 2017. The trial evaluated the efficacy and safety of three dose regimens of tezepelumab as an add-on therapy in patients with a history of asthma exacerbations and uncontrolled asthma receiving inhaled corticosteroids/long-acting beta-agonist with or without oral corticosteroids and additional asthma controllers versus placebo. The trial showed annual asthma exacerbation rate reductions of 62 percent, 71 percent and 66 percent in the tezepelumab arms receiving either 70 mg or 210 mg every four weeks or 280 mg every two weeks compared to placebo (p<0.001 for all comparisons), respectively. These results were observed independent of baseline blood eosinophil count or other T2 inflammatory biomarkers. The most common adverse events were asthma-related, nasopharyngitis, headaches and bronchitis.

About the PATHFINDER Program

Building on the Phase 2b PATHWAY trial, the Phase 3 PATHFINDER program was initiated in the fourth quarter of 2017 with two pivotal trials NAVIGATOR and SOURCE. The program includes additional planned mechanistic and long-term safety trials.

NAVIGATOR is a Phase 3 multicenter, randomized, double-blinded, parallel-group, placebo-controlled trial designed to evaluate the efficacy and safety of a regular, subcutaneous administration of tezepelumab for 52 weeks in adult and adolescent patients with severe asthma inadequately controlled despite treatment with inhaled corticosteroid (ICS) plus one additional asthma controller medication.

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 beta-agonist (LABA), and chronic treatment with maintenance oral corticosteroid (OCS) therapy.

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 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 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 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 or others could identify safety, side effects or manufacturing problems with its products after they are on the market. 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 it 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 manufacturing facilities 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. 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 acquire other companies or products and to integrate the operations of companies 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 or 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.

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References

1. The Global Asthma Network. The Global Asthma Report 2014. [Online]. Available at: http://www.globalasthmanetwork.org/publications/Global_Asthma_Report_2014.pdf [Last accessed 07 August 2018].
2. 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; 24: 14009.
3. World Allergy Organization. The management of severe asthma: economic analysis of the cost of treatments for severe asthma 2013. http://www.worldallergy.org/educational_programs/world_allergy_forum/anaheim2005/blaiss.php (accessed 10 July 2017).
4. Adelphi real world respiratory disease specific programme. [Asthma patient data file]. Bollington, UK. Uncited raw data,

cited with permission 2011–2014.
5. Peters SP, Ferguson G, Deniz Y, et al. Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. Respir Med. 2006: 100(7):1139-51.
6. Fernandes AG, Souza-Machado C, Coelho RC et al. Risk factors for death in patients with severe asthma. J Bras Pneumol. 2014; 40(4): 364-372.
7. Gauvreau GM, O'Byrne PM, Boulet LP, et al. Effects of an anti-TSLP antibody on allergen-induced asthmatic responses. N Engl J Med 2014;370:2102–10.
8. Shaw DE, Sousa AR, Fowler SJ, et al. Clinical and inflammatory characteristics of the European U-BIOPRED adult severe asthma cohort. Eur Respir J 2015; 46(5): 1308–21.
9. Fahy JV. Type 2 inflammation in asthma--present in most, absent in many. Nat Rev Immunol 2015; 15(1): 57–65.
10. Fajt ML, Wenzel SE. Development of New Therapies for Severe Asthma. Allergy Asthma Immunol Res 2017; 9(1): 3–14.

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