Tezepelumab Significantly Reduced Asthma Exacerbations For A Broad Population Of Patients With Severe Uncontrolled Asthma

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Novel Investigational Drug is Designed to Block Thymic Stromal Lymphopoietin (TSLP) - An Upstream Driver of Inflammation in Asthma

Results Published Today in New England Journal of Medicine and to be Presented at European Respiratory Society (ERS) Congress Next Week

THOUSAND OAKS, Calif., Sept. 6, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca (NYSE:AZN) today announced results from the PATHWAY Phase 2b trial of tezepelumab that showed a significant reduction in the annual asthma exacerbation rate compared with placebo in patients with severe, uncontrolled asthma. Tezepelumab is a novel anti-thymic stromal lymphopoietin (TSLP) monoclonal antibody being developed by MedImmune, AstraZeneca's global biologics research and development arm, in collaboration with Amgen.

The trial results were published today in the *New England Journal of Medicine (NEJM)*, and will be followed by an oral presentation at the European Respiratory Society (ERS) International Congress 2017 in Milan on Sept. 12, 2017.[1]

The PATHWAY trial achieved its primary efficacy endpoint, showing annual asthma exacerbation rate reductions of 61 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, respectively ($p<0.001$ for all comparisons to placebo). In the trial, tezepelumab was given as an add-on therapy to patients with a history of asthma exacerbations and uncontrolled asthma despite receiving inhaled corticosteroids/long-acting beta-agonists with or without oral corticosteroids (OCS) and additional asthma controllers.[2]

Significant and clinically meaningful reductions in the exacerbation rate were observed independent of baseline blood eosinophil count or other type 2 [(T2) referred to as Th2 in the *NEJM* publication] inflammatory biomarkers. Tezepelumab also demonstrated improvements in lung function at all doses and in asthma control at the two higher doses ($p<0.05$ for all comparisons to placebo). The incidence of adverse events was similar between the tezepelumab and placebo groups. The most common adverse events (≥5 percent) in tezepelumab-treated patients were asthma, nasopharyngitis, headaches and bronchitis.[2] Future studies in large populations of patients will be important in confirming the results demonstrated in this trial.

"These efficacy results confirm the hypothesis that TSLP is an important mediator of inflammation in severe asthma," said Jonathan Corren, M.D., David Geffen School of Medicine, UCLA and Principal Investigator of the PATHWAY trial. "Due to its activity early in the inflammatory cascade, tezepelumab may be suitable for patients with both T2 and non-T2 driven asthma, including those ineligible for current biologic therapies which only target the T2 pathway."

"The responses seen with tezepelumab in the PATHWAY trial show promise for a novel therapeutic option with the potential to impact multiple downstream inflammatory pathways associated with asthma," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We are committed to leveraging our deep understanding of inflammatory pathways to develop innovative treatments that address significant unmet medical needs."

TSLP is an upstream epithelial cytokine that drives multiple inflammatory pathways in various diseases, including asthma. TSLP is active in the regulation of T2 immunity; however, it may also play a role in non-T2 driven inflammation by activating or signaling to many types of cells, such as mast cells, basophils, natural killer T cells, innate lymphoid cells and neutrophils.[3-7] Therefore, TSLP has been identified as a potential therapeutic target across a broad asthma population.[3,7]

About Severe Asthma

Asthma affects 315 million individuals worldwide,[8] 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 OCS.[9,10]

Severe, uncontrolled asthma is debilitating, with patients experiencing frequent exacerbations and significant limitations on lung function.[11,12]

There is a significant physical and socio-economic burden of severe, uncontrolled asthma with these patients accounting for 50 percent of asthma-related costs.[13]

T2 inflammation-driven (T2 high) asthma is present in more than 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).[14,15] Conversely, approximately one-third of patients with severe asthma do not present with features of an activated T2 inflammatory pathway, and no biologic treatment options currently exist for these patients whose non-T2 driven disease is uncontrolled on established standard of care therapies.[16]

About Tezepelumab

Tezepelumab is the first of a new kind of potential medicines targeting TSLP.[7] Tezepelumab is a human anti-TSLP monoclonal antibody that is designed to specifically bind to human TSLP and prevent interaction with its receptor complex.[7] Blocking TSLP with tezepelumab may prevent the release of pro-inflammatory cytokines by immune cells targeted by TSLP. Due to its activity early in the inflammation cascade, tezepelumab may be suitable for a broad population of patients with severe, uncontrolled asthma, including in those whose asthma is not T2 driven.

About the PATHWAY Trial

The PATHWAY trial was a Phase 2b 52-week, randomized, double-blind, parallel group, placebo-controlled trial designed to evaluate the efficacy and safety of three dose regimens of tezepelumab, 70 mg and 210 mg every four weeks and 280 mg every two weeks, as an add-on therapy in patients

with a history of asthma exacerbations and uncontrolled asthma receiving inhaled corticosteroids/long-acting beta-agonists with or without OCS and additional asthma controllers.[17]

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.

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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.

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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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