Update On SOURCE Phase 3 Trial For Tezepelumab In Patients With Severe, Oral Corticosteroid-Dependent Asthma

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THOUSAND OAKS, Calif., Dec. 21, 2020 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca today announced the SOURCE 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.

The 48-week trial assessed the efficacy and safety of the potential new medicine tezepelumab compared to placebo in 150 severe asthma patients who required maintenance use of oral corticosteroids (OCS) on top of standard of care (SoC). Tezepelumab's effect on other efficacy parameters was similar to those observed in previous studies, including the registrational Phase 3 NAVIGATOR study. Further analyses of the data are ongoing.

The safety profile of tezepelumab in the trial was consistent with previous trials. Detailed results from the SOURCE trial will be presented at a future medical meeting.

"The recent results from our NAVIGATOR trial were impressive, both in terms of the overall clinical data and the reduction in exacerbation rate with tezepelumab treatment, and we continue to work with AstraZeneca on planned regulatory filings in 2021. While the SOURCE results were surprising, they provide important insights into the use of oral corticosteroids and the patients who are receiving them, which we look forward to exploring further," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "On initial review, the study design may have contributed to the results observed on the primary endpoint."

On November 10th, 2020, AstraZeneca and Amgen announced positive results from the NAVIGATOR Phase 3 trial which met the primary endpoint and demonstrated a statistically significant and clinically meaningful reduction in the annualized asthma exacerbation rate (AAER) in a broad population of patients with severe asthma, including those with low levels of eosinophils.

Tezepelumab is a potential first-in-class medicine that blocks the action of thymic stromal lymphopoietin (TSLP), an epithelial derived cytokine that plays a key role across the spectrum of asthma inflammation.[2,3]

Severe asthma is a complex, heterogenous disease and many patients continue to face debilitating symptoms despite receiving standard of care inhaled medicines and currently approved biologics.[5-8]

In September 2018, the US Food and Drug Administration granted Breakthrough Therapy Designation for tezepelumab in patients with severe asthma, without an eosinophilic phenotype.[4] Tezepelumab is being developed by AstraZeneca in collaboration with Amgen (see AstraZeneca and Amgen collaboration below).

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.[2,3,12]

TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles.[2,3] Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity.[3,12] Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control. [3,12] 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.[3,12]

PATHFINDER Clinical Trial Program
Building on the positive Phase 2b PATHWAY trial, the Phase 3 PATHFINDER program included two trials, the registrational NAVIGATOR study and SOURCE.[12-15] The program includes additional planned mechanistic and long-term safety trials.

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.[13] In the trial, patients were randomized to receive tezepelumab 210mg 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.[13]

The primary efficacy endpoint was the percentage reduction from baseline in the prescribed daily OCS maintenance dose at 48 weeks while not losing asthma control. Secondary endpoints included the effect of tezepelumab on annualized asthma exacerbation rate, lung function, asthma control, quality of life, work productivity and activity impairment. The SOURCE trial population included approximately 35% of subjects with high (≥ 300 cells/µL) and 65% with low (<300 cells/µL) blood eosinophil counts.[13]

Patient's OCS dose was optimized during an 8-week optimization period. For the first eight weeks of the 48-week treatment period, patients remained on their optimized OCS dose. OCS dose reduction was started at week four, with the possibility of a dose reduction every 4 weeks if asthma control was maintained up until week 40. From week 40 onwards, patients remained on the OCS dose reached at week 40 (or earlier if the OCS dose reduction failed because of clinical deterioration) or remained on complete OCS elimination if possible.[13]

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 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.[15]

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.[16]

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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