TEZSPIRE™ (TEZEPELUMAB-EKKO) NOW AVAILABLE IN THE UNITED STATES FOR THE TREATMENT OF SEVERE ASTHMA

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New Biologic Therapy Available for Broad Population of Severe Asthma Patients Without Phenotype or Biomarker Limitations

THOUSAND OAKS, Calif., Jan. 13, 2022 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca today announced TEZSPIRE™ (tezepelumab-ekko) is now available for shipment to wholesalers in the U.S. TEZSPIRE was approved by the U.S. Food and Drug Administration (FDA) on Dec. 17, 2021 for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.[1]

"Severe asthma has historically been a complex disease for patients to manage and for physicians to treat," said Murdo Gordon, executive vice president of Global Commercial Operations at Amgen. "About 60 percent of people have multiple drivers of disease and may not respond well to existing treatments. TEZSPIRE was approved for a broad population of people living with severe asthma, and we look forward to getting this important medicine into the hands of millions of patients who have had an unmet medical need."

TEZSPIRE is a first-in-class biologic for severe asthma that acts at the top of the inflammatory cascade by targeting thymic stromal lymphopoietin (TSLP), an epithelial cytokine.[2] TEZSPIRE is the first and only biologic for severe asthma that does not have a phenotype—eosinophilic or allergic—or biomarker limitation within its approved label.[4-11] TEZSPIRE consistently and significantly reduced asthma attacks across Phase 2 and 3 clinical trials which included a broad population of severe asthma patients irrespective of key biomarkers, including blood eosinophil counts, allergic status and fractional exhaled nitric oxide (FeNO).[2,3]

The most common adverse reactions (incidence ≥3% and more common than placebo) of TEZSPIRE are pharyngitis, arthralgia, and back pain.[1]

Amgen and AstraZeneca are committed to providing appropriate patients who are prescribed TEZSPIRE with affordable access to the medicine. The Tezspire Together Program offers provider and patient product resources and support, including information related to coverage, reimbursement and distribution. For more information about the Tezspire Together Program, call 1-888-TZSPIRE (1-888-897-7473) or visit Tezspire.com.

Amgen and AstraZeneca also provide patient assistance for TEZSPIRE for qualifying individuals with no or limited drug coverage by providing free medicines through the Tezspire Patient Assistance Program. For additional information, patients and caregivers may contact Tezspire Together.

TEZSPIRE™ (tezepelumab-ekko) U.S. Indication
TEZSPIRE is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.

TEZSPIRE is not indicated for the relief of acute bronchospasm or status asthmaticus.

TEZSPIRE™ (tezepelumab-ekko) Important Safety Information
CONTRAINDICATIONS
Known hypersensitivity to tezepelumab-ekko or excipients.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Hypersensitivity reactions (e.g., rash and allergic conjunctivitis) can occur following administration of TEZSPIRE. These reactions can occur within hours of administration, but in some instances have a delayed onset (i.e., days). In the event of a hypersensitivity reaction, initiate appropriate treatment as clinically indicated and then consider the benefits and risks for the individual patient to determine whether to continue or discontinue treatment with TEZSPIRE.

Acute Asthma Symptoms or Deteriorating Disease
TEZSPIRE should not be used to treat acute asthma symptoms, acute exacerbations, acute bronchospasm, or status asthmaticus.

Abrupt Reduction of Corticosteroid Dosage
Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with TEZSPIRE. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Parasitic (Helminth) Infection
It is unknown if TEZSPIRE will influence a patient's response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with TEZSPIRE. If patients become infected while receiving TEZSPIRE and do not respond to anti-helminth treatment, discontinue TEZSPIRE until infection resolves.

Live Attenuated Vaccines
The concomitant use of TEZSPIRE and live attenuated vaccines has not been evaluated. The use of live attenuated vaccines should be avoided in patients receiving TEZSPIRE.

ADVERSE REACTIONS
The most common adverse reactions (incidence ≥3%) are pharyngitis, arthralgia, and back pain.

USE IN SPECIFIC POPULATIONS
There are no available data on TEZSPIRE use in pregnant women to evaluate for any drug-associated risk of major birth defects, miscarriage, or other

adverse maternal or fetal outcomes. Placental transfer of monoclonal antibodies such as Tezepelumab-ekko is greater during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy.

Please see the TEZSPIRE full Prescribing Information.

You may report side effects related to AstraZeneca products by clicking here.

About the NAVIGATOR and the PATHFINDER Clinical Trial Program

In addition to the Phase 2b PATHWAY trial, the Phase 3 PATHFINDER program included two trials, NAVIGATOR and SOURCE. [2,12-14] The program includes additional mechanistic and long-term safety trials.[15]

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 standard of care (SoC). SoC was treatment with medium- or high-dose inhaled corticosteroids (ICS) plus at least one additional controller medication with or without daily oral corticosteroid treatment. The trial population included approximately equal proportions of patients with high (≥300 cells per microliter) and low (<300 cells per microliter) 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.[2]

The primary efficacy endpoint was the AAER during the 52-week treatment period. Key secondary endpoints included the effect of TEZSPIRE on lung function, asthma control and health-related quality of life.[3]

As part of prespecified analyses, the AAER over 52 weeks was also assessed in patients grouped by baseline blood eosinophil count, FeNO level and serum specific immunoglobin E (IgE) status (perennial aeroallergen sensitivity positive or negative).[3] These are inflammatory biomarkers used by clinicians to inform treatment options and involve tests analyzing a patient's blood (eosinophils/IgE) and exhaled air (FeNO).

The most frequently reported adverse events for TEZSPIRE were nasopharyngitis, upper respiratory tract infection and headache.[2]

NAVIGATOR is the first Phase 3 trial to show benefit in severe asthma irrespective of eosinophils by targeting TSLP.[2] These results support the U.S. Food and Drug Administration Breakthrough Therapy Designation granted to TEZSPIRE in September 2018 for patients with severe asthma, without an eosinophilic phenotype. In July 2021, TEZSPIRE was the first and only biologic to be granted Priority Review in the U.S. for the treatment of asthma by the FDA.

Patients who participated in our Phase 3 clinical trials were eligible to continue in DESTINATION, a Phase 3 extension trial assessing long-term safety and efficacy.[16]

About TEZSPIRE™ (tezepelumab-ekko)

TEZSPIRE is a 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, TEZSPIRE 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.[3,17] TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles.[3,17] Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity.[3,18] Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control.[3,18] By working at the top of the cascade, TEZSPIRE helps stop inflammation at the source and has the potential to treat a broad population of severe asthma patients.[3,18]

TEZSPIRE is also in development for other potential indications including chronic obstructive pulmonary disease, chronic rhinosinusitis with nasal polyps, chronic spontaneous urticaria and eosinophilic esophagitis (EoE). In October 2021, tezepelumab was granted Orphan Drug Designation by the FDA for the treatment of EoE.

About Severe Asthma

Globally, there are approximately 2.5 million patients with severe asthma who are uncontrolled or biologic eligible, with approximately 1 million in the U.S. Many patients with severe asthma have an inadequate response to currently available biologics and oral corticosteroids and thus fail to achieve asthma control.[19-24] 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.[20-22] Patients with severe uncontrolled asthma have twice the risk of asthma-related hospitalizations.[25,26] There is also a significant socio-economic burden with these severe uncontrolled asthma patients accounting for 50% of asthma-related costs.[28]

Multiple inflammatory pathways are involved in the pathogenesis of asthma.[27-29] Eosinophilic asthma, and more broadly, T2 inflammation-driven asthma, accounts for about two-thirds of patients with severe asthma.[29] These patients are typically characterized as having elevated levels of inflammatory biomarkers, including blood eosinophils, serum IgE and FeNO.[30,31] 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.[31]

About the Amgen and AstraZeneca Collaboration

In 2020, Amgen and AstraZeneca updated the 2012 collaboration agreement for TEZSPIRE. 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, Amgen and AstraZeneca will jointly commercialize TEZSPIRE in North America. Amgen will record product sales in the U.S., with AstraZeneca recording its share of U.S. profits as Collaboration Revenue. Outside of the U.S., AstraZeneca will record product sales, with Amgen recording profit share as Other/Collaboration revenue.

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.

Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average and is also part of the Nasdaq-100 index. In 2021, Amgen was named one of the 25 World's Best Workplaces™ by Fortune and Great Place to Work™ and one of the 100 most sustainable companies in the world by Barron's.

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., Kyowa-Kirin Co., Ltd., or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), the Five Prime Therapeutics, Inc. acquisition, or the Teneobio, Inc. acquisition, 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 our business, 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 our 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 we project. Our results may be affected by our 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 our products and global economic conditions. In addition, sales of our 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, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our 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 our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. 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, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our 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 we have acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Global economic conditions may magnify certain risks that affect our business. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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References

1. *TEZSPIRE* (tezepelumab) U.S. prescribing information; 2021.
2. Corren J, et al. Tezepelumab in adults with uncontrolled asthma [supplementary appendix; updated April 18, 2019]. *N Engl J Med*. 2017; 377: 936-946.

3. Menzies-Gow A, *et al*. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. *N Engl J Med*. 2021;384:1800-1809. DOI: 10.1056/NEJMoa2034975.
4. Hanania NA, *et al*. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. *Ann Intern Med*. 2011;154 (9): 573-82.
5. Yancey SW, *et al*. Disease burden and efficacy of mepolizumab in patients with severe asthma and blood eosinophil counts of ≥150-300 cells/μL. *Respir Med*. 2019; 151: 139-141.
6. FitzGerald JM, *et al*. Predictors of enhanced response with benralizumab for patients with severe asthma: pooled analysis of the SIROCCO and CALIMA studies. *Lancet Respir Med*. 2018; 6 (1): 51-64.
7. Castro M, *et al*. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. *N Engl J Med*. 2018; 378 (26): 2486-2496.
8. Ortega HG, *et al*; on behalf of the MENSA Investigators. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med*. 2014;371(13):1198-207.
9. Bleecker ER, *et al*, on behalf of the SIROCCO study investigators. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting beta2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. *Lancet* 2016: 388 (10056): 2115-2127.
10. FitzGerald JM, *et al*, on behalf of the CALIMA study investigators. Benralizumab, an anti-interleukin-5 receptor alpha monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet.* 2016: 388(10056): 2128-2141.
11. Wenzel S, *et al*. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. *Lancet.* 2016 Jul 2;388(10039):31-44
12. Menzies-Gow A, *et al*. NAVIGATOR: a phase 3 multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma. *Respir Res.* 2020; 21: 266.
13. Wechsler ME, *et al*. Oral corticosteroid-sparing effect of tezepelumab in adults with severe asthma. *Am J Respir Crit Care Med.* 2021;203:A1197.
14. Weschler ME, *et al.* SOURCE: A Phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel group trial to evaluate the efficacy and safety of Tezepelumab in reducing oral corticosteroid use in adults with oral corticosteroid dependent asthma. *Respir Res.* 2020; 21: 264.
15. Clinicaltrials.gov. Efficacy and Safety of Tezepelumab in Participants With Severe Chronic Rhinosinusitis With Nasal Polyposis (WAYPOINT). Available at: https://clinicaltrials.gov/ct2/show/NCT04851964. [Last accessed: July 2021].
16. 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: July 2021].
17. Varricchi G, et al. Thymic Stromal Lymphopoietin Isoforms, Inflammatory Disorders, and Cancer. *Front Immunol.* 2018; 9: 1595.
18. Li Y, et al. Elevated Expression of IL-33 and TSLP in the Airways of Human Asthmatics In Vivo: A Potential Biomarker of Severe Refractory Disease. *J Immunol*. 2018; 200: 2253–2262.
19. Centers for Disease Control and Prevention. Most Recent National Asthma Data. Available at: https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm. Accessed September 23, 2021
20. Wenzel S. Severe Asthma in Adults. Am J Respir Crit Care Med. 2005;172;149–60.
21. Chung KF, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J.* 2014; 43: 343–73.
22. 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.
23. Chastek et al. *J Manag Care Spec Pharm* 2016;22:848-861.
24. Chen et al. *Curr Med Res Opin* 2018;34(12):2075-2088.
25. 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.
26. World Allergy Organization (WAO). The management of severe asthma: economic analysis of the cost of treatments for severe asthma. Available at: https://www.worldallergy.org/educational_programs/world_allergy_forum/anaheim2005/blaiss.php [Last accessed: April 2021].
27. 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.
28. 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.
29. 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.
30. 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: April 2021].
31. Fahy JV. Type 2 inflammation in asthma--present in most, absent in many. *Nat Rev Immunol.* 2015; 15: 57-65.

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