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Tezspire met both co-primary endpoints in the Phase III WAYPOINT trial in patients with chronic rhinosinusitis with nasal polyps

Tezspire demonstrated a statistically significant and clinically meaningful reduction in nasal polyp size and reduced nasal congestion compared to placebo

Positive high-level results from the Phase III WAYPOINT trial in patients with chronic rhinosinusitis with nasal polyps (CRSwNP [nasal polyps]) showed that AstraZeneca and Amgen's *Tezspire* (tezepelumab) demonstrated a statistically significant and clinically meaningful reduction in the size of nasal polyps and reduced nasal congestion compared to placebo.

WAYPOINT is a randomised, double-blind trial that evaluated the efficacy and safety of *Tezspire* administered subcutaneously compared to placebo in adults with severe CRSwNP. Participants in the trial were symptomatic despite treatment with standard of care (intranasal corticosteroids [INCS]).[1]

Dr. Joseph Han, Vice Chair of Rhinology & Endoscopic Sinus and Skull Base Surgery, and Allergy, Otolaryngology-Head and Neck Surgery, Eastern Virginia Medical School, US, and co-primary investigator in the trial, said, "Chronic rhinosinusitis with nasal polyps negatively impact patients' daily lives with obstructions leading to disturbances in smell, taste and sleep as well as pain and fatigue. The impressive data from the WAYPOINT trial demonstrate tezepelumab's potential as a new treatment for patients whose lives are disrupted by this debilitating disease."

Dr. Brian Lipworth, Professor of Allergy and Pulmonology, Scottish Centre for Respiratory Research, and Tayside Rhinology Ear, Nose and Throat Clinic, Ninewells Hospital University of Dundee in Scotland, UK, and co-primary investigator in the trial, said, "Patients diagnosed with nasal polyps continue to experience significant burden including repeat surgeries and frequent treatment with high doses of oral corticosteroids, which are associated with serious systemic side effects. The tezepelumab data are clinically meaningful and offer patients with nasal polyps hope for a potential new treatment option that may reduce the burden on patients and healthcare systems."

Sharon Barr, Executive Vice President, BioPharmaceuticals R&D said: "We are excited by the positive results from the Phase III WAYPOINT trial, which show that patients with nasal polyps strongly benefitted from treatment with tezepelumab. These results reinforce that tezepelumab's first-in-class mode of action, targeting TSLP at the top of the inflammatory cascade, effectively addresses the multiple drivers of epithelial-driven inflammatory diseases."

The safety profile and tolerability of *Tezspire* in this trial were consistent with the known profile of the medicine.

Full results will be shared with regulatory authorities and the scientific community at an upcoming medical meeting.

Tezspire is currently approved for the treatment of severe asthma in the US, EU, Japan, and nearly 60 countries across the globe.[2-5] It is approved as a single-use pre-filled syringe and auto-injector for self-administration in the US and EU.[2,3]

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Notes:

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP (nasal polyps))

CRSwNP is a complex inflammatory disorder, characterised by persistent inflammation of the nasal mucosa accompanied by benign growths, called nasal polyps.[6,7] Nasal polyps can block nasal passages and lead to breathing problems, difficulty in sense of smell, nasal discharge, facial pain, sleep disturbance and other adverse effects on quality of life.[8-10]

Epithelial dysfunction and inflammation are important characteristics of chronic rhinosinusitis and impede the ability of the epithelium to act as a physical and immunological barrier against the external environment.[11] Thymic stromal lymphopoietin (TSLP) is an epithelial cytokine that has been implicated in shared pathophysiological processes underlying severe asthma and CRSwNP.[10,12]

Current treatments for CRSwNP include intranasal and/or systemic corticosteroids, surgery and biologics.[8,13-16]

Phase III WAYPOINT trial

WAYPOINT is a double-blind, multi-centre, randomised, placebo-controlled, parallel group trial designed to evaluate the efficacy and safety of tezepelumab in adults with severe CRSwNP.[1] Participants received tezepelumab or placebo, administered via subcutaneous injection. The trial also included a post-treatment follow-up period of 12-24 weeks for participants who completed the 52-week treatment period.[1]

The co-primary endpoints of the trial, were change from baseline in total nasal polyp size, measured by the endoscopic total Nasal Polyp Score, and change from baseline in bi-weekly mean nasal congestion, measured by

the participant reported Nasal Congestion Score evaluated as part of the daily Nasal Polyposis Symptom Diary.[1] Key secondary endpoints included loss of smell; improvement in disease specific health-related quality of life as measured by SinoNasal Outcome Test (SNOT-22) score; Lund-Mackay score; time to surgery decision and/or systemic corticosteroids for nasal polyposis; time to nasal polyposis surgery decision; time to systemic corticosteroids for nasal polyposis; Nasal Polyposis Symptom Diary total symptom score and, in the population with co-morbid asthma, pre-bronchodilator FEV1 at Week 52.

Tezepelumab

Tezepelumab is being developed by AstraZeneca in collaboration with Amgen as a first-in-class human monoclonal antibody that inhibits the action of TSLP, a key epithelial cytokine that sits at the top of multiple inflammatory cascades and is critical in the initiation and persistence of allergic, eosinophilic, and other types of endothelial inflammation associated with severe asthma and other inflammatory diseases.[17,18]

TSLP is released in response to multiple triggers (including allergens, viruses and other airborne particles) associated with asthma, CRSwNP, chronic obstructive pulmonary disease (COPD), eosinophilic esophagitis (EoE) and other diseases.[18,19] Expression of TSLP is increased in these patients and has been correlated with disease severity.[10,17] Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of exacerbations and improved disease control.[17,18,20] Tezepelumab acts at the top of the inflammatory cascade and research indicates that targeting TSLP released by the airway epithelium may be a potential approach to treating diseases of the lower airways in the future.[17,21,22]

Tezspire is approved in the US, the EU and nearly 60 countries for the add-on maintenance treatment of adult and paediatric patients aged 12 years and older with severe asthma.[2-5]

Beyond CRSwNP, tezepelumab is also in development for other potential indications including COPD and EoE.[23,24] In October 2021, tezepelumab was granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) for the treatment of EoE. In July 2024, the U.S. FDA granted a Breakthrough Therapy Designation for tezepelumab for the add-on maintenance treatment of patients with moderate to very severe COPD characterised by an eosinophilic phenotype.

Amgen collaboration

In 2020, Amgen and AstraZeneca updated a 2012 collaboration agreement for *Tezspire*. Both companies will continue to share costs and profits equally after payment by AstraZeneca of a mid single-digit inventor 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 commercialise *Tezspire* in North America. Amgen will record product sales in the US, with AZ recording its share of US profits as Collaboration Revenue. Outside of the US, AstraZeneca will record product sales, with Amgen recording profit share as Other/Collaboration revenue.

AstraZeneca in Respiratory & Immunology

Respiratory & Immunology, part of AstraZeneca BioPharmaceuticals is a key disease area and growth driver to the Company.

AstraZeneca is an established leader in respiratory care with a 50-year heritage and a growing portfolio of medicines in immune-mediated diseases. The Company is committed to addressing the vast unmet needs of these chronic, often debilitating, diseases with a pipeline and portfolio of inhaled medicines, biologics and new modalities aimed at previously unreachable biologic targets. Our ambition is to deliver life-changing medicines that help eliminate COPD as a leading cause of death, eliminate asthma attacks and achieve clinical remission in immune-mediated diseases.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca

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