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**_Tezspire_ demonstrates positive Phase III results in eosinophilic esophagitis across both co-primary and all key secondary endpoints**

***Statistically significant and clinically meaningful disease and symptom improvements compared to placebo maintained through week 52***

***Efficacy in a third epithelial-driven inflammatory disease supports broad potential of Tezspire***

Positive high-level results from the Phase III CROSSING trial in patients with eosinophilic esophagitis (EoE) showed that AstraZeneca and Amgen's *Tezspire* (tezepelumab) demonstrated statistically significant and clinically meaningful improvements across both co-primary and all key secondary endpoints at week 24, which were sustained through week 52 in both doses tested. The co-primary endpoints were histologic remission and the frequency and severity of dysphagia (difficulty swallowing) compared to placebo. The safety profile of *Tezspire* in the trial was generally consistent with its approved indications.

CROSSING is a randomised, double-blind trial that evaluated the efficacy and safety of *Tezspire* administered subcutaneously every four weeks compared to placebo in adults and adolescents with symptomatic and uncontrolled EoE while on maintenance therapy.[1] In the trial, the first co-primary endpoint, histologic remission, was defined as having a low count of peak eosinophils in the esophageal tissue.[1] The second co-primary endpoint, the frequency and severity of dysphagia, was assessed using the patient-reported Dysphagia Symptom Questionnaire (DSQ) and measured as a mean change from baseline in DSQ score.[1]

EoE is a chronic and progressive epithelial-driven inflammatory disorder of the esophagus affecting more than 470,000 people in the US, with the prevalence increasing five-fold since 2009.[2,3] The inflammation of the esophagus can lead to dysphagia, food impaction and esophageal narrowing.[2] Nearly half of patients, including adolescents, do not achieve adequate disease control with current first-line treatments, which include dietary restriction, swallowed topical corticosteroids and proton pump inhibitors.[4-6] For patients, the risk of food moving slowly or becoming stuck can make daily meals difficult and stressful.[7]

Arjan Bredenoord, MD, Gastroenterologist and professor at the Amsterdam University Medical Center, Amsterdam, The Netherlands, and primary investigator in the trial, said: "Despite the availability of first-line therapies or dietary interventions, many patients with eosinophilic esophagitis still experience substantial burden, including difficulty swallowing food, and emotional and daily-life impacts of the disease. The impressive results from the CROSSING trial sustained over 52 weeks demonstrate that tezepelumab, taken every four weeks, could provide a new approach to treating this disease, with the potential to help more patients achieve remission and symptom improvement."

Sharon Barr, Executive Vice President, BioPharmaceuticals R&D said: "The positive results of the Phase III CROSSING trial reinforce our confidence in the differentiated mechanism of action of *Tezspire,* which has now demonstrated clinically meaningful efficacy in a third epithelial-driven inflammatory disease. Epithelial science represents an important and rapidly evolving area in respiratory and immunology medicine, and we look forward to sharing these

results at an upcoming medical meeting and with regulatory authorities as quickly as possible."

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

*Tezspire* is a first-in-class human monoclonal antibody that inhibits the action of thymic stromal lymphopoietin (TSLP), a key epithelial cytokine that sits at the top of multiple inflammatory cascades. *Tezspire* is currently approved for the treatment of severe asthma in the US, EU, China, Japan and more than 70 countries across the globe, and for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in the US, EU, China and Japan. The Phase III JOURNEY and EMBARK trials evaluating *Tezspire* in chronic obstructive pulmonary disease (COPD) are ongoing.[8,9]

## Notes

### Eosinophilic Esophagitis (EoE)

EoE is a chronic and progressive epithelial-driven inflammatory disorder of the esophagus with prevalence growing across the world.[2,3] It is characterised by inflammation, remodelling and esophageal epithelial dysfunction.[2] Epithelial dysfunction and inflammation are important characteristics of EoE and impede the ability of the epithelium to act as a physical and immunological barrier against the external environment.[2]

The most common symptoms of EoE include difficulty and pain when swallowing, food becoming stuck in the esophagus (which may require emergency medical interventions), nausea and vomiting, abdominal or chest pain, poor appetite and difficulty sleeping.[2,10,11] Many patients, including adolescents, experience a substantial impact on their quality of life including significant anxiety related to swallowing and choking, depression, and decreased work/school productivity.[12,13]

Patients are often treated with proton pump inhibitors or swallowed topical corticosteroids to manage inflammation.[2,4] Nearly half of patients with EoE will not respond to standard first-line therapies or dietary treatment.[5,6] Existing treatment options, including those targeting downstream mediators, may not fully address epithelial-driven inflammation.[14,15]

### CROSSING

CROSSING is a randomised, double-blind, placebo-controlled, multi-centre, parallel-group, Phase III trial designed to evaluate the efficacy and safety of *Tezspire* administered subcutaneously every four weeks, compared to placebo in patients aged 12-80 years with symptomatic and histologically active EoE.[1] A total of 368 patients were randomised in a 1:1:1 ratio to receive either a low or high dose of *Tezspire* or placebo.[1]

The co-primary endpoints analysed at Week 24 were the proportion of patients with histologic remission, defined as a peak esophageal eosinophil count less than or equal to six eosinophils per high-power field, and mean changes from baseline in the DSQ.[1] The peak eosinophil count is obtained when biopsies of the tissue of the esophagus are examined under a microscope.[1] A count of 15 or more peak eosinophils per high power microscopic field measured by esophageal biopsy is often the cutoff used to diagnose EoE.[16,17] The DSQ captures the presence and severity of dysphagia symptoms in a daily diary with a four-item patient-reported questionnaire; the score is calculated over 14-day periods, ranging from zero to 84, with a higher score indicating more severe dysphagia.[1]

Key secondary endpoints assessed histologic remission and dysphagia symptoms at Week 52; changes in endoscopic disease features (EoE-EREFS) and histologic severity and extent (EoE-HSS) at Weeks 24 and 52; as well as endoscopic response, inflammatory remission and total endoscopic remission at Week 52.[1]

In the trial, patients were allowed to remain on background medications for EoE, including proton pump inhibitors and swallowed topical corticosteroids, provided that they were stable prior to entry and during the treatment period.[1]

**Tezepelumab and TSLP**
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.[18] TSLP is critical in the initiation and persistence of allergic, eosinophilic and other types of epithelial-driven inflammation associated with severe asthma, CRSwNP, COPD and EoE.[19-20]

TSLP is released by the epithelium in response to environmental triggers.[18] Across these disease states, the expression of TSLP is increased and correlates with disease severity.[18-22]

*Tezspire* is approved as a single-use pre-filled syringe and auto-injector for self-administration in the US, EU, China and Japan. Since 2021, more than 100,000 patients have been treated with *Tezspire* for severe asthma.[23]

In October 2021, *Tezspire* was granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) for the treatment of EoE.[24] Beyond EoE, *Tezspire* is also being explored in Phase III trials in COPD.[8,9]

**Amgen Collaboration**
The 2012 Collaboration Agreement between Amgen and AstraZeneca has been amended and updated over time. For *Tezspire*, both companies 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 agreement, Amgen and AstraZeneca jointly commercialise *Tezspire* in the US. Amgen records product sales in the US, with AZ recording its share of US profits as Alliance Revenue. Outside of the US, AstraZeneca records product sales.

**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/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, 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.

**Contacts**

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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**Matthew Bowden**
**Company Secretary**
**AstraZeneca PLC**