This announcement contains inside information

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Tozorakimab met primary endpoint in both OBERON and TITANIA Phase III trials in patients with COPD

First-ever IL-33-targeting biologic to demonstrate statistically significant and highly clinically meaningful reductions in COPD exacerbations in two replicate Phase III clinical trials

Positive high-level results from the Phase III OBERON and TITANIA trials in patients with chronic obstructive pulmonary disease (COPD) showed that tozorakimab reduced the annualised rate of moderate-to-severe COPD exacerbations compared with placebo, in the primary population of former smokers, and in the overall population, which included former and current smokers, and patients across all blood eosinophil* counts and all stages of lung function severity. Tozorakimab was generally well tolerated with a favourable safety profile.

Tozorakimab is a potential first-in-class monoclonal antibody targeting interleukin-33 (IL-33), that uniquely inhibits the signalling of the reduced and oxidised forms of IL-33, offering the potential to both reduce inflammation and disrupt the cycle of mucus dysfunction that contribute to COPD worsening.[1-4] In the OBERON and TITANIA trials, tozorakimab was studied in patients with COPD still experiencing exacerbations while on inhaled standard of care.[5,6] Patients received tozorakimab 300mg or placebo on top of standard of care once every four weeks.

Nearly 400 million people are diagnosed with COPD, a heterogenous and progressive disease and the 3rd leading cause of death globally.[7,8] Even when on inhaled standard of care, more than 50% of patients experience exacerbations, putting them at an increased risk of cardiopulmonary events and mortality.[9-12]

Frank Sciurba, MD, FCCP, Professor of Pulmonary and Critical Care Medicine, University of Pittsburgh, Chief Investigator of LUNA programme, said: "These trial results suggest that targeting the IL-33 pathway with tozorakimab delivers meaningful clinical benefit in a trial representing a broad COPD population, independent of smoking status and eosinophilic levels. COPD has long been a difficult-to-treat disease with inherent heterogeneity and significant unmet need, with up to half of patients worldwide at risk of exacerbations, hospitalisations, cardiopulmonary events, and death - underscoring the importance of these results for advancing COPD science."

Sharon Barr, Executive Vice President, BioPharmaceuticals R&D, AstraZeneca, said: "Today's tozorakimab results deliver the first two confirmatory Phase III trials for an IL-33 biologic, which is a major scientific advancement in COPD, the world's third leading cause of death. Tozorakimab works in a fundamentally different way from other biologics, inhibiting the signalling of the reduced and oxidised forms of IL-33 to both decrease inflammation and disrupt the cycle of mucus dysfunction that are key disease drivers in COPD."

The full results from the OBERON and TITANIA clinical trials will be shared with the scientific community at an upcoming medical meeting.

Additional Phase III trials of tozorakimab in COPD, PROSPERO and MIRANDA, are ongoing.[13,14] Tozorakimab is also being studied in a Phase III trial for severe viral lower respiratory tract disease and in a Phase II trial in asthma.[15,16]

**eosinophil: a type of white blood cell, which at increased levels may contribute to inflammation in respiratory diseases.*[17]

Notes

COPD

COPD, the third leading cause of death (excluding COVID-19) worldwide, is a progressive respiratory condition characterised by persistent airflow limitation and chronic inflammation of the airways.[8,18] Common symptoms include breathlessness, chronic cough and excess mucus production.[18] These symptoms can worsen over time and contribute to ongoing inflammation and bronchoconstriction, making it difficult to breathe and increasing the risk of COPD exacerbations.[18] These COPD exacerbations have a profound impact on the lives of those with the disease, accelerating disease progression, increasing hospitalisations, and increasing the risk of future cardiopulmonary events - including heart attacks, all of which can be life-threatening.[12,18] In the US, exacerbations cause more than 2,500 emergency department visits per day.[19] Only 50% of COPD patients live more than 3.5 years after their first severe exacerbation.[20]

Phase III LUNA programme

Tozorakimab's Phase III COPD development programme includes four clinical trials: OBERON, TITANIA, PROSPERO and MIRANDA.

OBERON and TITANIA

OBERON and TITANIA are replicate Phase III double-blind, placebo-controlled trials investigating the efficacy and safety of tozorakimab in adults with symptomatic COPD with a history of ≥2 moderate or ≥1 severe COPD exacerbations in the 12 months prior to enrolment. A total of 2,306 patients were randomised in both trials irrespective of blood eosinophil count or smoking status and across all stages of lung function severity.[5,6] Patients were placed on a regimen of tozorakimab 300mg once every four weeks, or placebo over the course of 52 weeks on top of inhaled therapy.

Prior to enrolment, patients received standard-of-care inhaled maintenance therapy for at least three months. The primary endpoint is annualised rate of moderate-to-severe COPD exacerbations in former smokers with COPD. A key secondary endpoint measured the annualised rate of moderate-to-severe COPD exacerbations in the overall population of former and current smokers.[5,6]

PROSPERO

The PROSPERO trial is a randomised, long-term extension clinical trial that enrolled patients who completed the OBERON or TITANIA trials. The primary endpoint is the annualised rate of severe COPD exacerbations in former smokers with COPD over 104 weeks. A total of 1,713 patients were randomised in this trial.[13] Results are expected in H1 2026.

MIRANDA

MIRANDA is a Phase III double-blind, placebo-controlled trial investigating the efficacy and safety of tozorakimab in adults with symptomatic COPD with a history of ≥2 moderate or ≥1 severe COPD exacerbations in the 12 months prior to enrolment. A total of 1,454 patients were randomised in this trial, recruited irrespective of blood eosinophil count or smoking status and across all stages of lung function severity.[14] Patients were placed on a regimen of tozorakimab 300mg once every two weeks, or placebo over the course of 52 weeks on top of inhaled therapy.

Prior to enrolment, patients received standard-of-care inhaled maintenance therapy for at least three months. The primary endpoint is annualised rate of moderate-to-severe COPD exacerbations in former smokers with COPD. Key secondary endpoints include the

annualised rate of moderate-to-severe COPD exacerbations in the overall population of former and current smokers.[14] Results are expected in H1 2026.

Tozorakimab

Tozorakimab is being developed by AstraZeneca as a first-in-class potent human immunoglobulin monoclonal antibody that binds to interleukin (IL-33). Tozorakimab targets the top of the inflammatory cascade uniquely inhibiting IL-33 signalling in two ways, thereby suppressing inflammation and disrupting the cycle of mucus dysfunction.[1] Tozorakimab is currently being investigated in Phase III clinical trials for COPD and severe viral lower respiratory tract disease and a Phase II trial for asthma.[5,6,13-16] Tozorakimab was granted Fast Track Designation by the US Food and Drug Administration for the treatment of severe viral lower respiratory tract disease in November 2023 and for COPD in December 2024.[21]

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 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.

Contacts

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

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This announcement contains information that AstraZeneca PLC is obliged to make public pursuant to the EU Market Abuse Regulation (596/2014) and the assimilated EU Market Abuse Regulation (596/2014) as it forms part of the law of the United Kingdom by operation of the European Union (Withdrawal) Act 2018. This announcement was submitted for publication, through the agency of the contact person(s) set out above, at 7:00 GMT on 27 March 2026.