RNS Number : 0175B
AstraZeneca PLC
20 April 2026

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Tozorakimab met primary endpoint in Phase III MIRANDA trial in patients with COPD

Third positive pivotal Phase III clinical trial of AstraZeneca's IL-33-targeting biologic further demonstrates its benefits in COPD

Positive high-level results from the pivotal Phase III MIRANDA trial showed potential first-in-class tozorakimab demonstrated a statistically significant and clinically meaningful reduction in the annualised rate of moderate-to-severe COPD exacerbations 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.

In MIRANDA, patients received tozorakimab 300mg or placebo on top of standard of care once every two weeks.[1] The trial enrolled patients with COPD still experiencing moderate-to-severe exacerbations while on inhaled standard of care.[1] These results follow an announcement in March of the positive high-level results from the pivotal Phase III OBERON and TITANIA trials studying tozorakimab at a four-week dosing interval.

Frank Sciurba, MD, FCCP, Professor of Pulmonary and Critical Care Medicine, University of Pittsburgh, Chief Investigator of LUNA programme said: "These results add to the growing body of evidence that indicates tozorakimab delivered meaningful clinical benefits for COPD patients who urgently need new treatment options. Up to half of patients today still experience exacerbations even when taking standard-of-care inhaled therapies, putting them at risk of serious health consequences including hospitalisation and even death."

Sharon Barr, Executive Vice President, BioPharmaceuticals R&D, AstraZeneca, said: "These data further demonstrate tozorakimab's exciting potential as a first-in-class biologic with a truly differentiated mechanism of action that inhibits the signalling of the reduced and oxidised forms of IL-33 to address underlying drivers of COPD. We look forward to sharing the data with regulators and the scientific community as soon as possible."

Tozorakimab was generally well tolerated with a favourable safety profile consistent with previous trials. The data will be submitted to regulatory authorities and shared with the scientific community at an upcoming medical meeting.

Nearly 400 million people are diagnosed with COPD, a heterogenous and progressive disease and the 3rd leading cause of death globally.[2,3] 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.[4-7]

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.[8-11]

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.[12,13]

**eosinophil: a type of white blood cell, which at increased levels may contribute to inflammation in respiratory diseases.*[14]

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.[3,15] Common symptoms include breathlessness, chronic cough and excess mucus production.[15] 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.[15] 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.[7,15] In the US, exacerbations cause more than 2,500 emergency department visits per day.[16] Only 50% of COPD patients live more than 3.5 years after their first severe exacerbation.[17]

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

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, including former and current smokers, and patients across all blood eosinophil counts and all stages of lung function severity.[18,19] 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.[18,19]

MIRANDA
MIRANDA is a Phase III double-blind, placebo-controlled trial investigating the efficacy and safety of tozorakimab in

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, including former and current smokers, and patients across all blood eosinophil counts and all stages of lung function severity.[1] 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. A key secondary endpoint measured the annualised rate of moderate-to-severe COPD exacerbations in the overall population of former and current smokers.[1]

PROSPERO
The PROSPERO trial is a randomised, long-term extension clinical trial that enrolled patients who completed the OBERON or TITANIA trials. PROSPERO has a different primary endpoint, which is the annualised rate of only severe COPD exacerbations (hospitalisations and death) in former smokers with COPD over 104 weeks. A total of 1,713 patients were randomised in this trial.[20]

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.[8] Tozorakimab is currently being investigated in a Phase III clinical trial for severe viral lower respiratory tract disease and a Phase II trial for asthma.[12,13] 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
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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

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