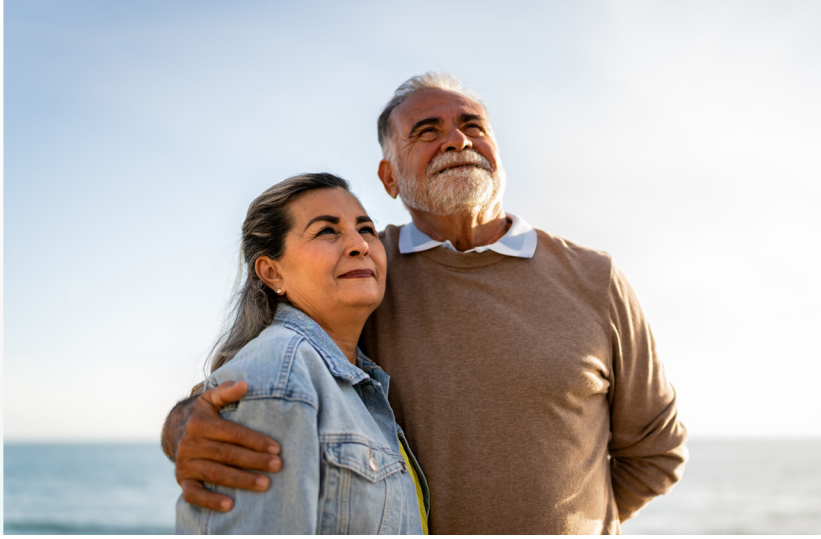
# AER-01:
# A Novel Approach in Obstructive Lung Disease Treatment



## The Mucus Obstruction Problem

Chronic lung diseases like Chronic Obstructive Pulmonary Disease (COPD) and asthma are often complicated by mucus obstruction, a problem that significantly impairs breathing. Pathologic mucus buildup in the airways blocks airflow and prevents medications from reaching their target areas.

Despite advances in obstructive lung treatments, such as bronchodilators, steroids, and biologics, many patients with moderate-to-severe COPD and asthma continue to suffer from persistent breathlessness and frequent flare-ups. Current treatments and those currently in development are focused on reversing bronchoconstriction using long-acting beta agonists and muscarinic antagonists to relax the muscles surrounding the airways; or corticosteroids to reduce overall airway inflammation; and biologics to treat cellular inflammation in airways. However, there are no treatments that have been specifically designed to treat the pathologic buildup of mucus in the airways.

Biologics like Dupilumab and Tezepelumab have shown some improvements in mucus plugging by reducing mucus production through reducing type 2 inflammation. However, they are relatively slow to work and do not necessarily clear all existing mucus plugs, leaving an unmet need in this area.[1]

AER-01 is the first drug specifically designed to target core mucus pathology and the mucus obstructions in COPD and asthma, breaking down the dense and sticky mucus that blocks airflow. Unlike biologics or other traditional treatments, AER-01 works directly on mucus to clear the mucus plugs, offering a novel solution to a persistent problem in respiratory care.

## The Unmet Need

In the United States, approximately 30 million people are living with COPD or asthma. Of those, 5 million people have moderate-to-severe COPD and another 1.5 million have severe asthma.[2] Among the higher risk groups, 30-50% show visible mucus obstruction on imaging, translating to roughly 2-3 million people with mucus-obstructive disease.[3] While mucus obstruction is primarily seen in more advanced cases, the broader diagnosed population of COPD and asthma patients in the US alone highlights a substantial potential market.

Mucus obstructions reduce lung function, contribute to chronic inflammation, are associated with more frequent exacerbations,[3] and are linked to higher mortality.[4] For patients, mucus obstructions result in a significant decrease in activities of daily living and high rate of hospitalizations.

> **This is more than just a nuisance—it's a persistent, harmful barrier to breathing and recovery, with no currently approved treatments.**

[1] Castro M, et al, Effect of dupilumab on exhaled nitric oxide, mucus plugs, and functional respiratory imaging in patients with type 2 asthma (VESTIGE): a randomised, double-blind, placebo-controlled, phase 4 trial. Lancet Respir Med. 2025 Mar;13(3):208-220. doi: 10.1016/S2213-2600(24)00362-X

[2] Centers for Disease Control and Prevention. (2023). Chronic Obstructive Pulmonary Disease (COPD). https://www.cdc.gov/copd/

[3] Wan E, et al. Airway Mucus Plugs on Chest Computed Tomography Are Associated with Exacerbations in COPD. Am J Respir Crit Care Med. 2024 Oct 29;211(5):814–22. doi: 10.1164/rccm.202403-0632OC.

[4] Diaz AA, Orejas JL, Grumley S, Nath HP, Wang W, Dolliver WR, Yen A, Kligerman SJ, Jacobs K, Manapragada PP, Abozeed M, Aziz MU, Zahid M, Ahmed AN, Terry NL, San José Estépar R, Kim V, Make BJ, Han MK, Sonavane S, Washko GR, Cho M, San José Estépar R. Airway-Occluding Mucus Plugs and Mortality in Patients With Chronic Obstructive Pulmonary Disease. JAMA. 2023 Jun 6;329(21):1832-1839. doi: 10.1001/jama.2023.2065.

# Why Existing Drugs Fall Short

Currently, two older drugs—Mucomyst® (N-acetylcysteine) and Pulmozyme® (dornase alfa)—are sometimes prescribed to thin mucus, particularly in respiratory conditions like cystic fibrosis. But neither were developed specifically for COPD or asthma.

- **Mucomyst has a strong odor and often causes bronchoconstriction and irritation, making it difficult for many patients to tolerate, and its clinical benefit in obstructive lung diseases is limited.[5]**
- **Pulmozyme works by breaking down DNA in mucus and helps to thin it in conditions like in cystic fibrosis. But in asthma or COPD, where the mucus composition is different, Pulmozyme doesn't work to break up or clear the mucus plugs.[6]**

In contrast, AER-01 directly targets the thick, sticky mucus by breaking apart the bonds that hold the mucus together, making it less elastic and easier to clear. This makes AER-01 much more effective at rapidly clearing mucus plugs compared to Mucomyst or Pulmozyme.[7] Importantly, AER-01 targets the common pathway in all mucus, regardless of whether it's COPD, asthma, cystic fibrosis or bronchiectasis.

# A Market with No Direct Competitor

AER-01 is entering a wide-open space as there is no other approved drug for mucus plug clearance in COPD and other mucus obstructive diseases including asthma, cystic fibrosis, and non-CF bronchiectasis. Existing therapies such as bronchodilators, anti-inflammatories, and biologics all play critical roles in managing these diseases but do not directly address mucus plugs.

- **Bronchodilators help open the airways by relaxing the muscles around the airways, improving airflow and easing breathing. However, they do not tackle the mechanical problem of mucus obstruction blocking patients' airways.**
- **Anti-inflammatories, such as steroids, aim to reduce inflammation in the airways, and are central to controlling asthma and COPD symptoms. However, patients who take inhaled or oral steroids continue to have mucus plugs in their airways.[8]**
- **Biologics like Dupilumab and Tezepelumab have shown promise in reducing inflammation and mucus production, particularly in type 2-driven asthma. These biologics target specific inflammatory pathways (e.g., IL-4, TSLP) to reduce mucus secretion, but their effects on clearing existing mucus plugs are slower and indirect. While biologics can reduce some mucus burden and improve airflow over weeks to months, AER-01 has a unique advantage by directly liquefying and dissolving mucus plugs within minutes of administration, offering rapid relief that the other treatments cannot.[1]**

AER-01 fits seamlessly into existing treatment regimens, complementing bronchodilators, anti-inflammatories, and biologics by directly addressing the mucus obstruction that these current therapies do not resolve. Its fast-acting mechanism provides immediate benefits, allowing it to clear the airway for better penetration of other therapies and improving overall lung function more quickly. This makes AER-01 potentially an ideal complementary treatment, not competing with but enhancing the efficacy of other respiratory drugs.

[5] Dekhuijzen, P. N. (2004). Antioxidant properties of N-acetylcysteine: their relevance in relation to chronic obstructive pulmonary disease. European Respiratory Journal, 23(4), 629-636.

[6] O'Donnell, A. E., Barker, A. F., Ilowite, J. S., & Fick, R. B. (1998). Dornase alfa in the treatment of airway mucus hypersecretion in asthma: a pilot study. Annals of Allergy, Asthma & Immunology, 80(1), 59-63.

[7] Addante A, Raymond W, Gitlin I, Charbit A, Orain X, Scheffler AW, Kuppe A, Duerr J, Daniltchenko M, Drescher M, Graeber SY, Healy AM, Oscarson S, Fahy JV, Mall MA. A novel thiol-saccharide mucolytic for the treatment of muco-obstructive lung diseases. Eur Respir J. 2023 May 25;61(5):2202022. doi: 10.1183/13993003.02022-2022.

[8] Dunican EM, Elicker BM, Gierada DS, Nagle SK, Schiebler ML, Newell JD, Raymond WW, Lachowicz-Scroggins ME, Di Maio S, Hoffman EA, Castro M, Fain SB, Jarjour NN, Israel E, Levy BD, Erzurum SC, Wenzel SE, Meyers DA, Bleecker ER, Phillips BR, Mauger DT, Gordon ED, Woodruff PG, Peters MC, Fahy JV; National Heart Lung and Blood Institute (NHLBI) Severe Asthma Research Program (SARP). Mucus plugs in patients with asthma linked to eosinophilia and airflow obstruction. J Clin Invest. 2018 Mar 1;128(3):997-1009. doi: 10.1172/JCI95693.

## Global Reach Through International Trials

AER-01 is currently being evaluated in a Phase 2a trial, enrolling patients with COPD in the UK, Australia, and New Zealand.

The trial is targeting patients with radiographically confirmed mucus obstruction, which ensures that Aer Therapeutics is testing the drug in the population it was designed to help. Aer is also using imaging to accurately assess the full scope and magnitude of mucus burden reduction. In addition, the trial is assessing functional improvements in lung function and in respiratory symptoms, important clinical and regulatory measures.

Across these countries and globally, more than 100 million chronic lung disease patients may suffer from mucus-related obstruction. Even conservative penetration into this population represents a multibillion-dollar revenue opportunity.

## Looking Ahead: Treating Earlier, Changing the Game

Currently, AER-01 is aimed at patients with moderate-to-severe disease—those who still struggle despite optimal use of inhalers, steroids, and biologics. But there's a long-term vision to expand beyond this population. By clearing mucus obstructions before they lead to chronic inflammation and lung remodeling, AER-01 could potentially become more than just a treatment of symptoms—it could help alter the course of disease. That's a significant shift—one that grows in impact as it adds interest from payers, enthusiasm from providers, and potential for long-term adoption.

Commercially, this means label expansion and market longevity. Clinically, it means better outcomes for patients who currently have few options.

## Conclusion

Airway mucus obstructions have only been overlooked because the ability to treat them has been limited. AER-01 is the solution to this persistent challenge in respiratory diseases which affects millions of people, reduces the effectiveness of existing drugs, and drives poor outcomes. Until now, no effective drug has been developed to treat them in COPD and asthma.

AER-01 is the first drug of its kind. It works differently. It addresses an unmet need and complements existing therapies, creating a larger opportunity than any other standalone treatments typically offer. With clinical trials underway, global markets in reach, and no direct competitors, AER-01 represents a first-in-class opportunity to change the standard of care for COPD and asthma.

**For investors, AER-01 is more than just a new drug.**
**It's a new frontier in the treatment of lung disease.**