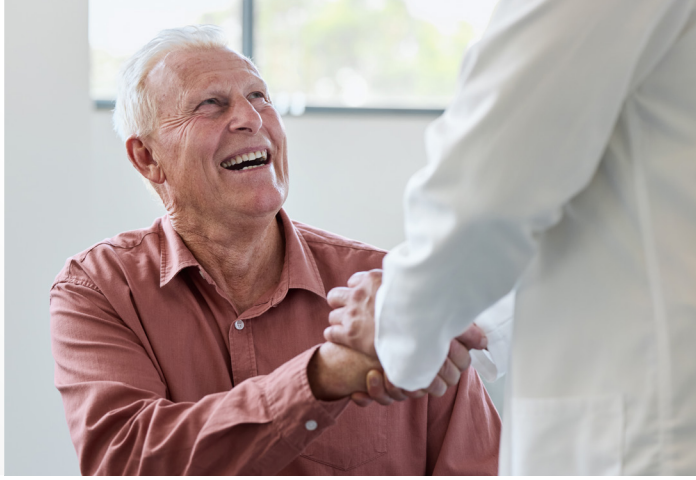
AER-01:
Innovating Along the Path to Regulatory Approval



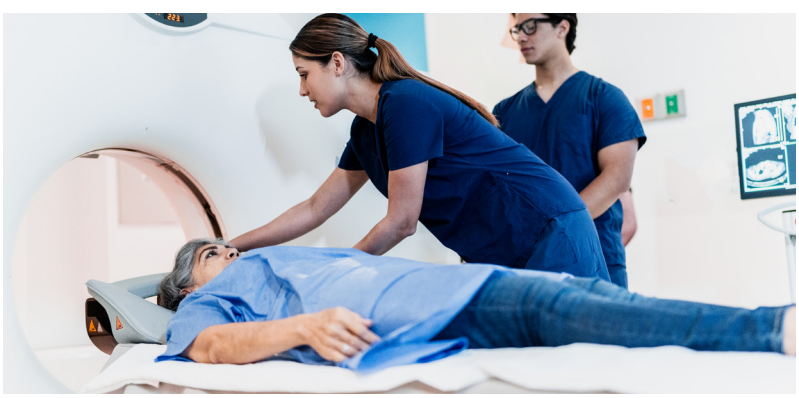
AER-01 is a next generation inhaled therapy specifically designed to dissolve mucus obstructions in patients with chronic obstructive lung diseases like COPD and asthma. While the scientific rationale and market need are compelling, strategic partners want to know more about the path of AER-01 to towards regulatory approval.

This paper outlines the strong preclinical foundation and intelligent clinical trial design that support AER-01's progress and potential to transform lung disease therapy.

A Clear Rationale Rooted in Strong Science

AER-01 targets obstructive mucus plugs in the airways — a significant clinical challenge in the treatment of chronic lung diseases. Mucus obstructions occur when excessive structural bonds are formed between mucin strands, transforming mucus into a dense, immovable barrier that contributes to breathlessness, hypoxemia, and increased risk of exacerbations.

Preclinical studies demonstrate that AER-01 breaks these structural bonds, effectively liquefying the obstruction and restoring airflow. While older mucolytics like Mucomyst (acetylcysteine) and Pulmozyme (dornase alfa) have been used in respiratory care to thin mucus, neither were designed for the biology of COPD and asthma. Additionally, recent biologics such as dupilumab and tezepelumab[1, 2] have shown promise in reducing mucus obstructions through modulation of type 2 inflammation. However, these effects are indirect, limited to select asthma phenotypes, and not designed to resolve established mucus obstructions.



Unlike therapies that work upstream to curb mucus production, AER-01 was designed to act directly at the site of an existing mucus obstruction by cleaving the disulfide bonds that stabilize the plug. When delivered by inhalation route, AER-01 has shown superior obstruction clearance in preclinical studies, with better onset and potency than older mucolytics, and thus laying a strong mechanistic foundation as it advances through clinical trials.

Phase 2a Clinical Trial: Designed to Deliver High-Quality Data

AER-01 is currently being evaluated in a multicenter, international Phase 2a proof-of-concept clinical trial enrolling patients in the UK, Australia, and New Zealand. The trial targets individuals with moderate-to-severe COPD who are likely to have high mucus burden. Mucus plugs will be quantified using high-resolution chest imaging at the start and end of the study to understand how the plugs respond to the drug. This tactical approach ensures that patient characteristics of those who respond to the drug are well understood for the future trials.

The study is measuring both functional and structural outcomes. The primary endpoint is the improvement in

[1] Castro, M., Papi, A., Porsbjerg, C., Lugogo, N. L., Brightling, C. E., González-Barcala, F. J., Bourdin, A., Ostrovskyy, M., Staevska, M., Chou, P. C., Duca, L., Pereira, A. M., Fogarty, C., Nadama, R., Zhang, M., Rodrigues, A., Soler, X., Sacks, H. J., Deniz, Y., ... Jacob-Nara, J. A. (2025). 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 Respiratory Medicine, 13(3), 208–220. https://doi.org/10.1016/S2213-2600(24)00362-X

[2] Nordenmark, L. H., Hellqvist, Å., Emson, C., Diver, S., Porsbjerg, C., Griffiths, J. M., Newell, J. D., Peterson, S., Pawlikowska, B., Parnes, J. R., Megally, A., Colice, G., & Brightling, C. E. (2023). Tezepelumab and mucus plugs in patients with moderate to-severe asthma. NEJM Evidence, 2(10), EVIDoa2300135. https://doi.org/10.1056/EVIDoa2300135

lung function (FEV1), and the secondary endpoints include improvements in patient-reported outcomes (PROs) such as the St. Georges Respiratory Questionnaire (SGRQ) and additional measures of spirometry, which are well-recognized in respiratory drug trials and provide clinically relevant measures of symptom burden and quality of life. AER-01's effect on mucus burden is also tracked through serial imaging before, during, and after treatment, offering direct evidence of the progression and impact of the drug.

Why Imaging Matters

One of the most significant innovations in this trial is utilization of imaging to understand the effects of the drug. In contrast to traditional respiratory trials that rely on symptoms or spirometry alone, AER-01's study design uses CT scans to quantify mucus burden. Imaging offers a way to visualize treatment response, allowing investigators to link any changes in lung function and quality of life with an observable and quantifiable reduction in mucus burden.

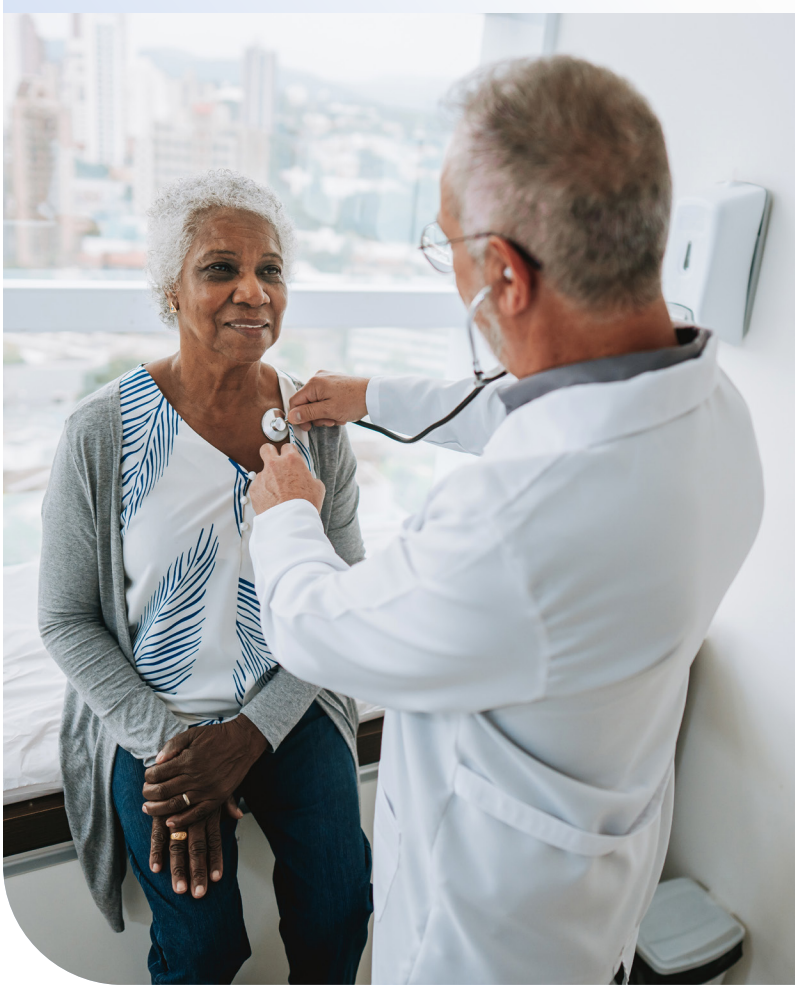
This direct link between mechanism and outcome is rare in respiratory drug development and provides strong evidence for regulatory and commercial stakeholders.

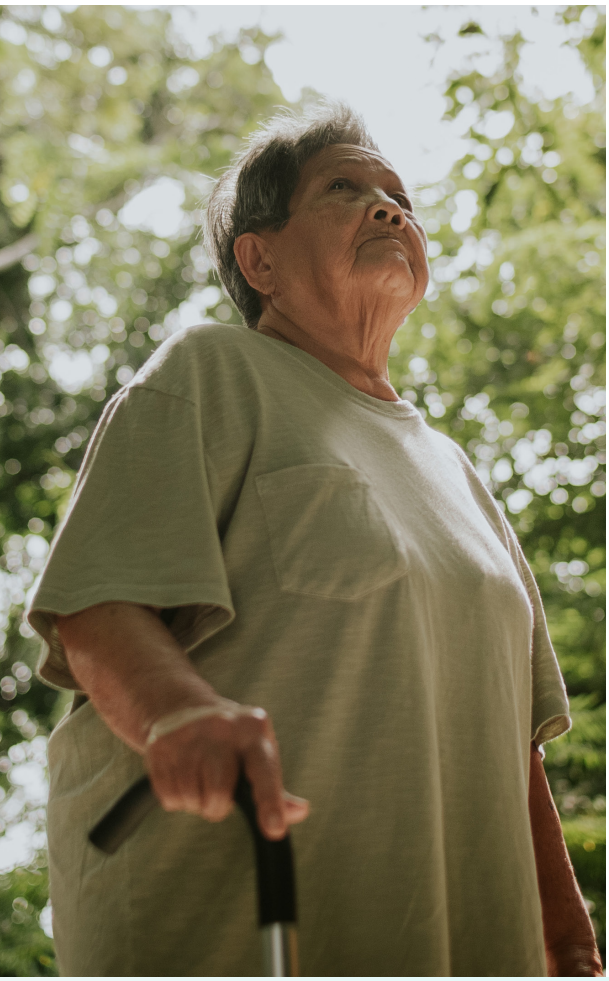
Regulatory Strategy and Forward Path

Aer Therapeutics has received ethics and CTA approvals in key international jurisdictions, enabling fast startup across trial sites. The study was designed in alignment with FDA and EMA guidance on COPD endpoints and may qualify for accelerated pathways if efficacy and tolerability are demonstrated. However, it's important to note that while the study was designed in alignment with these guidelines, Aer has not yet engaged directly with the FDA or EMA. However, our success in multiple other jurisdictions will also pave the regulatory path in the United States.

Combining imaging with functional data may support a differentiated regulatory strategy. These dual endpoints allow for both clinical relevance and mechanistic validation, strengthening the case for approval. Pending the results from Phase 2a, Aer expects to move into Phase 2b dose-ranging and Phase 3 trials and will be working with regulators to finalize study design. In its next development phase, Aer will have an opportunity to pursue either or both COPD and asthma indications.

> **"What sets this trial apart is how carefully we are looking at the effects of the drug on mucus plugs using imaging. By understanding the mucus burden of each patient and their response to the drug, we're learning how to design our next clinical study.**
>
> Dr. Irina Gitlin
> VP of Research & Development





A Successful Track Record of Execution

From early discovery through the execution of a global Phase 2a clinical trial, Aer Therapeutics has consistently prioritized science-driven decision-making and operational rigor.

In addition to its innovative clinical design, the AER-01 program is supported by a strong foundation of safety and manufacturing readiness. Toxicology studies in animal models showed no systemic side effects, and any local lung changes were limited and reversible. A Phase 1 study in 96 healthy human volunteers confirmed that AER-01 was safe and well-tolerated, with no serious adverse events or signs of airway irritation. From this study, the dose selected for Phase 2a was chosen based on how the drug performs in mucus samples from patients and how well it reaches the lungs.

On the manufacturing side, AER-01 is made through a simple, cost-effective process that has already been scaled up to multi-kilogram levels. Solution formulations of AER-01 are compatible with different types of nebulizers, maximizing its compatibility with existing delivery methods. Together, these technical elements reduce risk and position the program for regulatory and commercial success.

Conclusion

Historically, innovation in respiratory medicine has been limited to well-established mechanisms and re-formulations of existing treatments into new dosage forms. AER-01 is the opposite: a novel mechanism paired with innovative trial design that incorporates new and established endpoints.

By lysing mucus plugs, AER-01 opens airways, lets airflow reach distant areas on the lung, and removes the scaffold for accumulation of inflammatory cells. The value of AER-01 extends beyond symptom relief. By clearing mucus obstructions that block airflow and hinder drug delivery, AER-01 has the potential to enhance the effects of bronchodilators, corticosteroids, and antibiotics. This makes it a promising candidate not only as a stand-alone therapy but as a foundational component of multi-drug regimens. The mechanism of AER-01 may apply to other mucus-driven diseases like cystic fibrosis (CF) and non-CF bronchiectasis, chronic conditions where clearance of mucus obstructions could meaningfully improve outcomes and quality of life.

AER-01 is the evolution of a purpose-built program translating basic science into clinical care, combining novel biology, precision medicine, and rigorous development. It stands apart not just in what it treats, but how it's being brought forward, a clear example of what it means to innovate in the respiratory space. This innovative approach to targeting mucus obstructions provides a potentially high-return investment for investors, assuring that the path to regulatory approval is built on a solid foundation of scientific rigor, targeted trial design, and clear clinical endpoints.