aer therapeutics

Targeting mucus to improve lung health

Aer Therapeutics is a clinical stage biopharmaceutical company developing AER-01 to treat mucus plugs in muco-obstructive lung disease

AER Therapeutics

Targeting Mucus Obstruction to Improve Lung Health

2017-2021 — **Lab of John Fahy, MD (UCSF)**

- Established CT methods for mucus plugs quantitation in patients
- Rationally designed next-generation mucolytic drugs to target plugs
- Initial work supported by $18M in NIH funding, in collaboration with Stefan Oscarson (chemistry, UCD) and Anne Marie Healy (pharmaceutics, TCD)

2021 — **Aer Therapeutics Founded**

- Spinout from UCSF
- Nominated lead compound for development, AER-01

2022 — **$41M Series A**

- Canaan Partners, OrbiMed, Hatteras Ventures, Pappas Capital and the UCSF Foundation

2024 — **Completed Phase 1 SAD/MAD in Healthy Volunteers**

- AER-01 found to be safe and well-tolerated at doses up to 4x clinical target
- Established linear, dose-dependent pharmacokinetics

2025 — **First COPD Patient Dosed in Phase 2a**

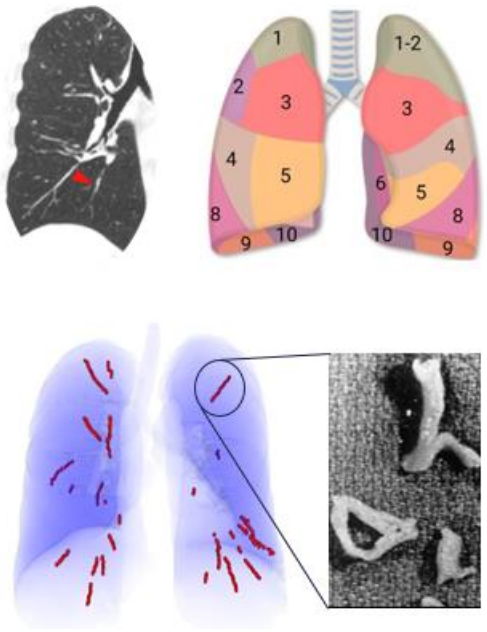
- AER-01-002 trial ongoing in Australia, New Zealand, and UK
- First clinical trial to use a CT-based mucus plug score as a precision medicine tool for enrollment.
- Top line data anticipated in 1H 2026

UCSF-University of California San Francisco
UCD-University College Dublin; TCD-Trinity College Dublin

Airway Mucus Plugs Drive Morbidity and Mortality in Severe COPD and Asthma

The ability to quantitatively assess mucus plugs has led to an understanding of their impacts on lung health

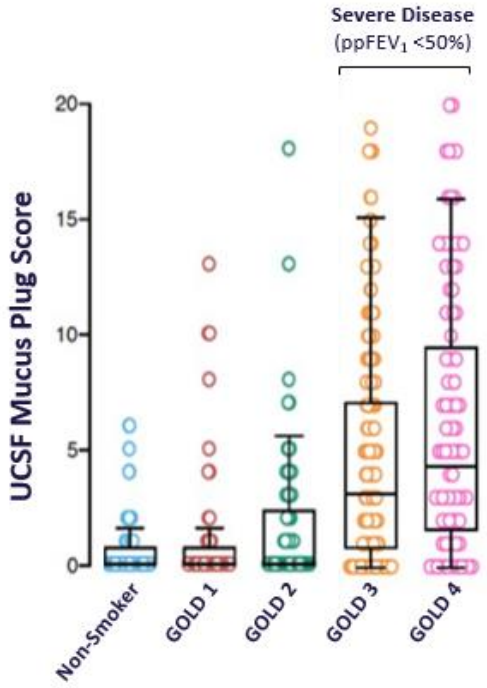
Mucus plugs can be identified and quantified by CT imaging



JCI The Journal of Clinical Investigation

Dunican EM et al. J Clin Invest 2018; 128(3).

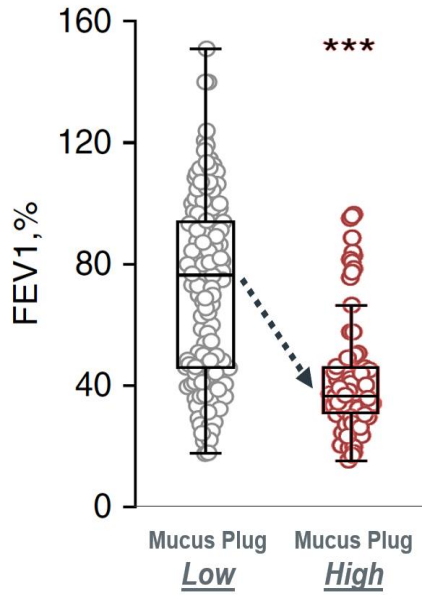
Mucus Plugs are Associated with *Increased Disease Severity*



RESPIRATORY AND CRITICAL CARE MEDICINE

Dunican EM et al. AJRCCM. 2021; 203(8).

Mucus Plugs are Associated with *Decreased Lung Function* and *Higher All-Casuse Mortality*



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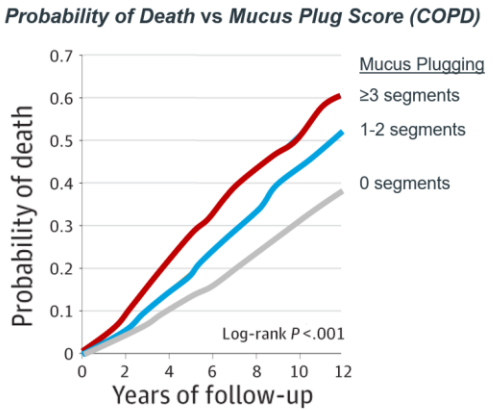


Mucus Plugs per Lung Segment	Mortality Rate (9-year, avg)
0	34.0% (±1.8%)
1-2	46.7% (±3.2%)
≥3	54.1% (±3.3%)

JAMA The Journal of the American Medical Association

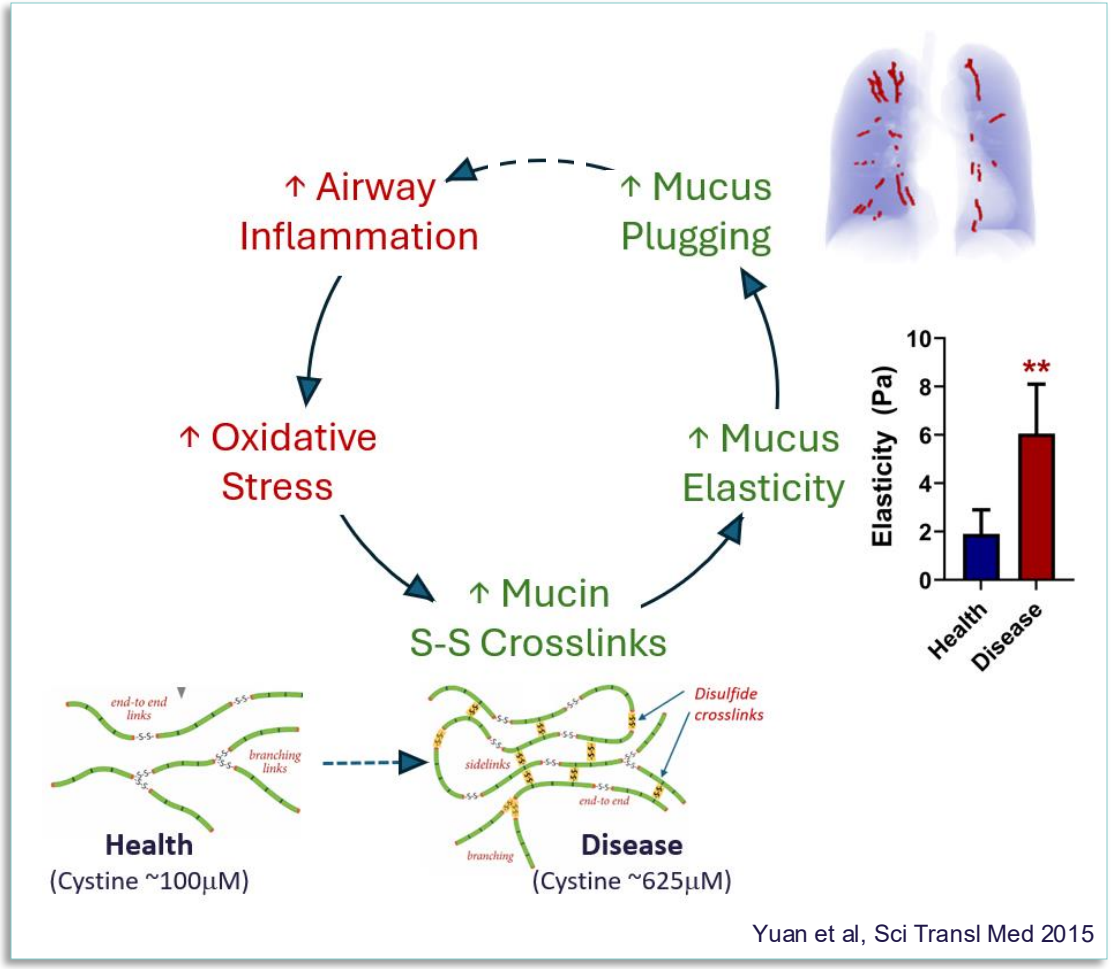
Diaz A, et al. JAMA 2023; 329(21)

SPIROMICS SARP aer therapeutics

Mechanism of Mucus Plug Formation and Design of a Novel Inhaled Mucolytic

Addressing the underlying biophysical changes in mucus that lead to plugging

Mucin cross-linking is the mechanism underlying plug formation



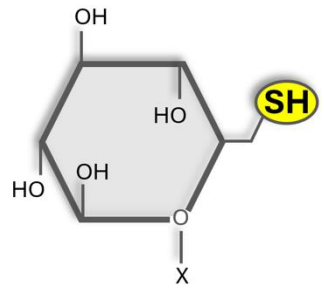
Yuan et al, Sci Transl Med 2015

AER-01 is rationally designed to break up mucin cross-links

Key Attributes of AER-01

- Thiol-modified saccharide scaffold
- Targets disulfide crosslinks in mucins
- Enhanced potency
  (> Mucomyst and > Pulmozyme)
- Well tolerated by inhalation
- Metabolically stable

- Scalable 3-step synthesis from commercial starting materials
- High aqueous solubility for nebulized formulations
- DPI compatible



Thiol-Saccharide

Clinical Development

Phase 2a topline results expected in H1 2026

Phase 1 SAD/MAD - clean safety profile

- **96 healthy volunteers successfully dosed in SAD/MAD (7d);**
- **Wide dose range tested (X-8X mg)**

Safety and Tolerability:

- No significant changes in lung function as measured by spirometry
- No SAEs or episodes of bronchoconstriction
- Daily dose that is **4x of Ph2a dose** cleared with no safety concerns
- Dose proportional exposure

Phase 1 safety profile allowed progression to Phase 2

Phase 2a PoC Study in COPD and Asthma – in progress

Study details

- Randomized, Double-blind, Placebo controlled, Parallel Group design
- Moderate-Severe COPD and Asthma
- 28-day treatment period

Innovative Precision Enrollment Strategy

- Select most responsive patient population – **those with high mucus burden and limited emphysema (COPD only)** – using CT lung imaging

Endpoints

- Primary: change in FEV_1 from baseline
- Secondary: i) change in CT mucus segment score, ii) change in SGRQ / ACQ6 score; safety
- Exploratory: changes in quantitative CT measures of mucus burden (plug size, shape, location); others

Advancing the treatment paradigm for mucus-mediated lung disease

Executive Summary

Aer Tx is a clinical-stage biopharma company

- **Spin out from UCSF** Airway Biology Lab
- **$41M Series A ($36M in Q4/22 and $5M extension in Q1/25)** raised to fund company through Phase 2a proof of concept (POC) study
- **Backed by premier syndicate**: Canaan, OrbiMed, Hatteras Ventures, and Pappas Ventures
- **Robust IP portfolio** licensed from UCSF (exclusivity through 2041)

Lead asset fexlamose (AER-01) and market opportunity

- **Rational drug design:** ability to **lyse mucus plugs** with a novel **thiol-saccharide** molecule **more potent than marketed mucolytics.**
- **Precision medicine approach** to identify COPD/asthma patients with highest potential benefit and **reduce clinical trial variability**.
- Primary market research of conservative product profile (14-day dosing) indicates > **$1 billion peak sales in U.S. alone**

Phase 2a clinical Proof of Concept study underway

- **14d and 13wk GLP toxicology studies completed**
- **CMC on track with drug substance at 50kg scale and stable drug product supplying Phase 2a**
- **Phase 1 SAD/MAD study completed in Q2/2024; excellent safety profile**
- **Phase 2a POC underway; topline results expected 1H/2026**

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