What You Need to Know

The Need for Innovation in Alpha-1 Antitrypsin Deficiency (Alpha-1)

Alpha-1: a genetic disease affecting the lungs

Alpha-1—also sometimes called AATD—is an underdiagnosed condition affecting ***~235,000 people worldwide***.[1,2]

The potential impact of Alpha-1 on the lungs*: Those living with Alpha-1 often experience progressive deterioration of the lung tissue and may develop emphysema, a common and serious form of chronic obstructive pulmonary disease (COPD).[1,3] In severe forms of the disease, patients can sometimes require lung transplantation.[4]

**Alpha-1 primarily affects the lungs and liver; the focus of this material is on the lungs. Most adults with Alpha-1 experience lung involvement (about 85%) and some have liver damage (about 15%).[3]*

There is an overall lack of awareness of Alpha-1 as a genetic cause of some forms of COPD.[5] An estimated ***90% of individuals with Alpha-1 are believed to be undiagnosed*** and therefore underserved, making them at higher risk for disease progression.[5,6]

The cause of Alpha-1: a missing protein

Alpha-1 is characterized by low levels or absence of a protective protein called ***alpha-1 antitrypsin (AAT)***.[3] The liver makes and releases this protein into the bloodstream. It helps to protect the lungs so they can function.[3]

Liver
Liver cells synthesize and secrete AAT into the blood stream[3]

AAT

Lung
AAT helps protect lung tissue from damage[3]

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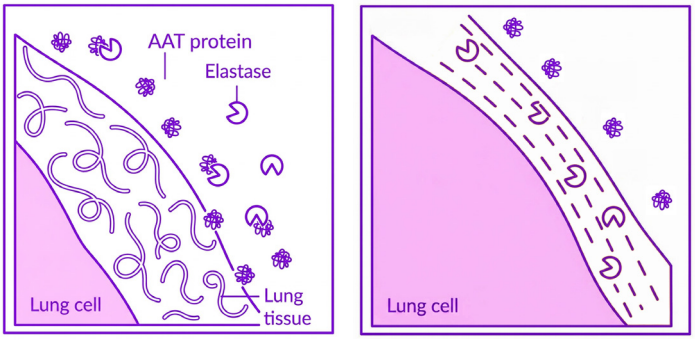
A closer look at how AAT helps to protect the lungs

AAT blocks ***neutrophil elastase and other proteases*** that can cause damage to lung tissue.[3,7] Neutrophil elastase is released from white blood cells to fight infection but if not tightly controlled by AAT, ***it can attack normal tissue in the lungs***.[3] The resulting tissue damage may cause difficulty breathing and can lead to conditions like COPD.[3,7] Environmental factors, such as exposure to tobacco smoke, chemicals, and dust, likely impact the severity of Alpha-1.[3]

A person not living with Alpha-1: AAT inactivates neutrophil elastase, thus helping to prevent damage to lung tissue.[3]



A person living with Alpha-1: With little or no AAT, neutrophil elastase is unchecked and can cause damage to the lung tissue. This can cause difficulty breathing, and lead to conditions like COPD.[3]

Addressing the unmet need

For nearly 40 years, weekly plasma-derived augmentation therapy (pdAAT) has been the standard-of-care for Alpha-1, intended to raise AAT levels in the lungs and bloodstream.[8,9] But unmet need persists as many people still have difficulty maintaining these levels within the normal range over time, potentially leaving them at risk for disease progression.[10]

The complexity of managing Alpha-1 may in part be rooted in a decades-long definition of less than or equal to 11 μM of serum AAT as the threshold under which risk for lung disease sets in.[11] This has since been challenged by other literature demonstrating that risk of lung disease may actually begin when patients are below normal levels of AAT, which in healthy individuals is 20 μM, especially when coupled with other environmental or lifestyle factors.[12]

People living with Alpha-1 need innovation and recognition of the large care gap that exists.

At Sanofi, we are leveraging our deep experience in both rare and respiratory diseases to pursue innovation in this space. We are working diligently to address persisting unmet needs in Alpha-1 grounded in our more than 40 years of supporting people with rare diseases.

References:

1. Learn About Alpha-1 Antitrypsin Deficiency. American Lung Association website. https://www.lung.org/lung-health-diseases/lung-disease-lookup/alpha-1-antitrypsin-deficiency/learn-about-alpha-1-antitrypsin-defiency. Updated January 2026. Accessed April 2026.
2. Smith G, Singh K. Alpha-1 Antitrypsin Deficiency: Navigating Challenges Through Collaborative Innovation. *Chest*. December 2024;166(6):1288-1290.
3. Alpha-1 antitrypsin deficiency. MedlinePlus Genetics website. https://medlineplus.gov/genetics/condition/alpha-1-antitrypsin-deficiency/. Accessed April 2026.
4. Zamora M, Ataya A. Lung and liver transplantation in patients with alpha-1 antitrypsin deficiency. *Ther Adv Chronic Dis*. July 2021;12_suppl:20406223211002988.
5. Pfeffer DN, Dhakne R, El Massad O, et al. Improving the Likelihood of Identifying Alpha-1 Antitrypsin Deficiency Among Patients With COPD: A Novel Predictive Model Using Real-World Data. *Chronic Obstr Pulm Dis*. 2025;12(1):1-11.
6. Aboussouan L, Stoller JK. Detection of alpha-1 antitrypsin deficiency: a review. *Respir Med*. March 2009;103(3):335-41.
7. Xiang S, Yang L, He Y, et al. Alpha-1 Antitrypsin as a Regulatory Protease Inhibitor Modulating Inflammation and Shaping the Tumor Microenvironment in Cancer. *Cells*. January 2025;14(2):88.
8. Wells AD, Woods A, Hilleman DE, et al. Alpha-1 Antitrypsin Replacement in Patients With COPD. *P T*. July 2019;44(7):412–415.
9. Treating and Managing Alpha-1 Antitrypsin Deficiency. American Lung Association website. https://www.lung.org/lung-health-diseases/lung-disease-lookup/alpha-1-antitrypsin-deficiency/treating-and-managing. Updated January 2026. Accessed April 2026.
10. Brantly ML, Kuhn BT, Farah HW, et al. Recombinant Alpha-1 Antitrypsin–Fc Fusion Protein INBRX-101 in Adults With Alpha-1 Antitrypsin Deficiency: A Phase 1 Study. *Chronic Obstr Pulm Dis*. June 2024;11(3):282–292.
11. Franciosi AN, Fraughen D, Carroll TP, et al. Alpha-1 antitrypsin deficiency: clarifying the role of the putative protective threshold. *Eur Respir J*. February 2022;59(2):2101410.
12. Mulkareddy V, Roman J. Pulmonary manifestations of alpha 1 antitrypsin deficiency. *Am J Med Sci*. July 2024;368(1):1-8.

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