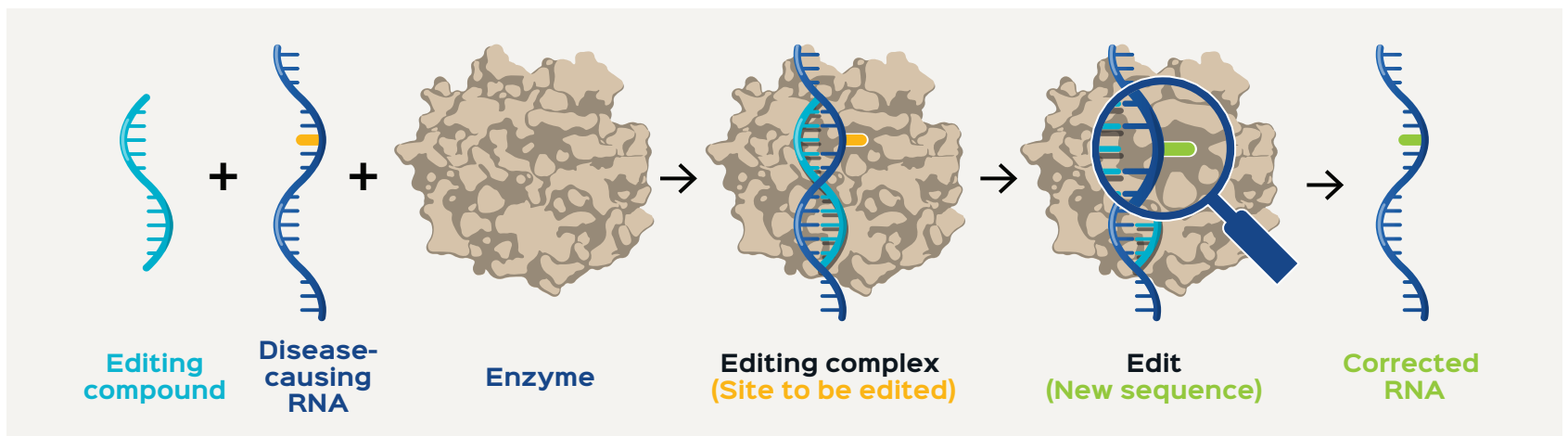




RNA Editing for Alpha-1 Antitrypsin Deficiency

What is RNA editing?

RNA editing is a new technology that corrects a disease-causing sequence in a person's RNA without making permanent changes to their DNA



RNA editing

- ▶ An **editing compound** interacts with the **disease-causing RNA** and an **enzyme** that naturally exists within the body
- ▶ The three components form an **editing complex**
- ▶ The enzyme makes a specific change or **edit** to the RNA, releasing the **corrected RNA**
- ▶ The **corrected RNA** leads to the production of M-AAT protein

RNA editing is designed to address key goals in the treatment of AATD

- ✓ Reduces Z-AAT protein aggregation in liver
- ✓ Releases circulating, functional M-AAT protein above expected therapeutic threshold (11 μM)
- ✓ Restores serum M-AAT protein to protect the lungs
- ✓ One approach for individuals with 'Z' mutations, whether they have liver disease, lung disease, or both
- ✓ Reversible, no permanent changes to DNA

What is Alpha-1 Antitrypsin Deficiency (AATD)?

AATD is an inherited genetic disorder that is commonly caused by a mutation that creates the 'Z allele' in the SERPINA1 gene, which results in the production of a protein called Z-AAT in place of the normal M-AAT protein.

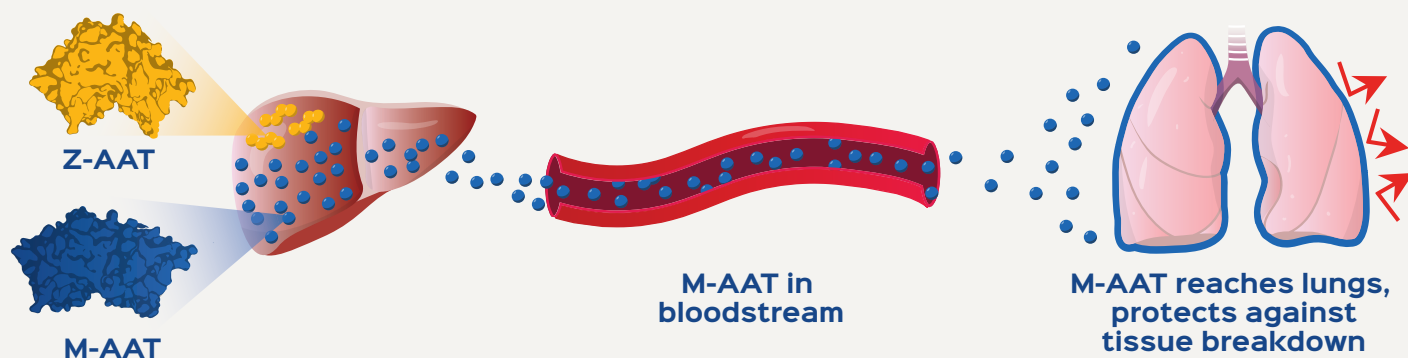
M-AAT protein is predominately produced by the liver. Production of Z-AAT protein by the liver can lead to aggregation of the protein and an inflammatory response, causing progressive liver disease. It also means the liver is not secreting M-AAT into the blood. Loss of M-AAT in the bloodstream can lead to lung disease.

RNA editing is designed to correct Z-AAT, replacing it with M-AAT

1) **Reduces** Z-AAT protein in the liver

2) **Releases** M-AAT in blood

3) **Restores** M-AAT in lungs



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