

Single-domain antibody inhibiting neutrophil elastase for the treatment of inflammatory lung diseases

KEY ACHIEVEMENTS

- Isolation and characterization of NbE201, first single-domain antibody inhibiting tightly, specifically, and competitively both human and murine NE
- NbE201 inhibits NE in sputa from patients with muco-obstructive lung diseases better than the endogenous NE inhibitor (AAT)
- PEGylated NbE201 is active (no aggregation) upon nebulization and spray-drying
- Topical NbE201 delivery prevents ARDS induced by the instillation of human NE in the lungs of mice

KEY COMPETITIVE ADVANTAGES

NbE201 is more potent, specific and cheaper to produce than AAT

UPCOMING CHALLENGES

- NbE201 optimization: higher affinity, improved pharmacokinetics, formulation ready for inhalation
- NbE201 non-GLP production
- Pre-clinical development in an indication to be identified

INTELLECTUAL PROPERTY

A PCT patent application has been filed on 28 June 2024 (PCT/EP2024/068395) and published under the publication number WO2025/003495.

PARTNERSHIP SOUGHT

Collaboration agreements to optimize NbE201 and take it into the clinic.

The human protease Neutrophil Elastase (NE) plays an essential role in the immune mechanism against bacterial infections and is a key mediator in tissue remodelling and inflammation. However, dysregulated extracellular release of NE in the lungs degrades proteins of the extracellular matrix and damages epithelial cells, promoting sustained and pathologic tissue inflammation, which leads to tissue destruction and loss of associated functions. Uncontrolled NE activity is associated with chronic obstructive pulmonary disease (COPD), Alpha-1 antitrypsin deficiency (AATD), bronchiectasis, cystic fibrosis, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), pulmonary arterial hypertension (PAH), idiopathic pulmonary fibrosis, and SARS-CoV-2-associated ARDS.

To date, only one small molecule inhibiting NE (Sivelestat) has been approved in Japan and Korea for the treatment of ALI. Its use is limited due to serious organ toxicity. Inhaled alpha1-antitrypsin (AAT), an endogenous inhibitor of NE, has shown limited efficacy. Because AAT is purified from human plasma, its production is expensive and limited.

There is an unmet medical need for new, highly specific, and stable NE inhibitors for the treatment of inflammatory lung diseases.

We have developed a highly potent (tight-binder), highly specific, and stable, single-domain antibody that inhibits competitively mouse and human NE (NbE201). NbE201 inhibits NE in sputa from muco-obstructive lung diseases patients more effectively than AAT and it prevents the development of acute respiratory distress syndrome induced by the instillation of NE in the lungs of mice. NbE201 has the potential to significantly improve the treatment of inflammatory lung diseases.