Acidic mammalian chitinase (AMCase) and chitotriosidase (CHIT1) are enzymatically active chitinases that have been implicated in the pathology of chronic lung diseases. Significantly elevated chitinolytic activity was demonstrated in asthma, chronic obstructive pulmonary disease (COPD) and interstitial lung diseases such as idiopathic pulmonary fibrosis (IPF) and sarcoidosis. Herein, we describe our studies on targeting chitinases with small molecules as a potential therapy for pulmonary diseases.

**CHITINASE INHIBITORS DEVELOPED BY OAT USED AS TOOLS IN OUR MOA AND POC STUDIES**

**INTRODUCTION**

Acidic mammalian chitinase (AMCase) and chitotriosidase (CHIT1) are enzymatically active chitinases that have been implicated in the pathology of chronic lung diseases. Significantly elevated chitinolytic activity was demonstrated in asthma, chronic obstructive pulmonary disease (COPD) and interstitial lung diseases such as idiopathic pulmonary fibrosis (IPF) and sarcoidosis. Herein, we describe our studies on targeting chitinases with small molecules as a potential therapy for pulmonary diseases.

**CHITINASE INHIBITORS DEVELOPED BY OAT USED AS TOOLS IN OUR MOA AND POC STUDIES**

**SAR STUDY**

In the course of our program over 2000 compounds have been designed and synthesized, resulting in OAT-870 as our advanced lead compound. Further optimization of drug-like properties and selectivity of OAT-870 yielded a clinical candidate OATD-01. The compound bears an additional methoxy group at the morpholine ring, which altogether reduced off-target activity toward dopamine transporter (DAT) 90%.

**OATD-01 EFFICACY IN BLEOMYCIN-INDUCED PULMONARY FIBROSIS MODEL IN MICE**

**CRYSTAL STRUCTURE OF OATD-01-CHIT1 COMPLEX**

**PHARMACOKINETIC PROFILE IN MICE**

**CONCLUSIONS**

**ACKNOWLEDGEMENTS**

*Preclinical research and clinical trials of a first-in-class development candidate in therapy of asthma and inflammatory bowel disease*

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**OATD-01, A Dual hAMCase and hCHIT Inhibitor as a Potential Therapeutic Agent for Treatment of Pulmonary Diseases.**

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