



Meta Anilide Inhibitors of MRTF

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Therapeutics and Vaccines
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OVERVIEW

A novel antifibrotic agent that potently inhibits MRTF-mediated extracellular signaling

- Directly treats the causes of fibrosis rather than just addressing its symptoms
- May prove useful for patients with scleroderma, IPF, liver cirrhosis, and Crohn's disease

BACKGROUND

Idiopathic pulmonary fibrosis (IPF) and scleroderma are two common fibrosis related disorders that cause progressive symptoms and may ultimately lead to death. IPF creates shortness of breath and cough predominately in older patients, while scleroderma commonly affects the skin and underlying tissues in younger patients, though it may eventually come to involve internal organs. The current treatment of IPF includes either nintedanib (which targets growth factor pathways) or pirfenidone (which inhibits collagen synthesis and reduces fibroblast proliferation). Each of these medicines suffer from the risk of significant adverse effects. Similarly, anti-inflammatory agents may lessen the symptoms of scleroderma, though with side effect risks that increase with prolonged use. So, a new therapeutic avenue is needed that decreases the fibrosis associated with these illnesses and which has an acceptable side effect profile.

INNOVATION

Researchers have invented an inhibitor of myocardin-related transcription factor (MRTF), which is known to play a crucial function in diseases that cause fibrosis. The inhibition of MRTF serum response factor (SRF) signaling decreases lung fibrosis, and inhibition of a MRTF transcription pathway involving both Rho GTPase and SRF has the potential to treat scleroderma. This novel

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approach directly treats fibrosis related illnesses rather than just addressing their symptoms, and they hold promise for diminished side effects when compared to existing agents. One study using the MRTF inhibitor showed decreased fibrosis and reversal of weight loss in a preclinical model of lung fibrosis. This class of drugs may also prove effective in addressing other ailments such as liver cirrhosis, Crohn's disease, and any other maladies that cause inappropriate fibrosis.