

Insilico starts Phase III trial of AI-discovered IPF therapy

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Rentosertib is a potentially first-in-class oral TNIK inhibitor being evaluated for idiopathic pulmonary fibrosis.



Insilico Medicine has initiated a Phase III clinical trial of rentosertib, its AI-discovered oral small-molecule TNIK inhibitor for idiopathic pulmonary fibrosis.

The Phase III trial marks the most advanced clinical milestone for Insilico's AI-enabled drug discovery platform. Rentosertib, formerly known as ISM001-055 or INS018_055, was developed through the company's Pharma.AI platform, combining AI-driven target discovery and generative chemistry.

This is relevant because idiopathic pulmonary fibrosis remains a progressive and life-limiting lung disease with limited treatment options. Current antifibrotic therapies may slow disease progression, but they do not reverse the underlying fibrotic process, leaving significant unmet need for differentiated disease-modifying therapies.

Rentosertib targets TNIK, a serine/threonine kinase implicated in fibrosis-driving and inflammation-related pathways, including Wnt, TGF- β , Hippo/YAP-TAZ, JNK and NF- κ B signalling. Insilico identified TNIK as a high-priority fibrosis target using multi-omics data, biological network analysis, causal inference, literature, patent intelligence and ageing-relevant target scoring.

The development is also significant for the AI drug discovery field. Rentosertib represents a programme where AI was used not only to optimise a molecule, but to identify the target, design the chemistry and support clinical development strategy. Its discovery-to-clinic journey has been published in Nature Biotechnology, while Phase IIa results were published in Nature Medicine.

The upcoming Phase III study is a prospective, randomised, double-blind, placebo-controlled, parallel-group trial. It is expected to enrol 320 patients with idiopathic pulmonary fibrosis across 47 centres in China. The study will evaluate once-daily rentosertib over 52 weeks.

The primary endpoint is annual rate of decline in forced vital capacity, while a key secondary endpoint is time to first occurrence of any disease progression event. These endpoints are relevant because lung function decline is central to IPF

progression and clinical deterioration.

In the Phase IIa GENESIS-IPF study, the 60 mg once-daily arm showed a mean forced vital capacity improvement of 98.4 mL at 12 weeks, compared with a decline of 20.3 mL in the placebo group. Treatment-emergent adverse event rates were similar across treatment arms, supporting advancement into longer and larger testing.

The programme remains investigational and has not been approved by any regulatory authority. The Phase III study will need to confirm whether the earlier safety profile and lung-function signal can translate into clinically meaningful benefit over a longer period.