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# Striking back at lung disease

**A treatment for fatal lung diseases such as idiopathic pulmonary fibrosis is being developed by Lung Therapeutics. The novel mechanism could have wider applications for other fibrotic diseases.**

A spin-out company in Austin, Texas could radically change the way we treat lung disease and conditions linked to fibrosis, such as idiopathic pulmonary fibrosis (IPF). Lung Therapeutics is developing a novel peptide drug that it expects will not only slow disease progression, but promote restoration of healthy lung function. Its novel mechanism enables the rebalancing of some fundamental biological signaling pathways. The drug may be the key to the treatment of a wider group of fibrosis-based conditions in multiple organs, such as cardiac fibrosis and scleroderma.

The company was co-founded in 2013 by Steven Idell and Andrew Mazar. Idell, a board-certified internist and pulmonologist, serves as the current CSO and is temple chair of pulmonary fibrosis at the University of Texas Health Science Center at Tyler. Mazar serves as the consulting head of product development and was recently director of the Center for Developmental Therapeutics at Northwestern University.

Since its first year, Lung Therapeutics has been led by CEO Brian Windsor, who has 18 years of experience in the formation and management of life-science-based technology ventures. He has rapidly developed the company's portfolio. Lung Therapeutics' first therapeutic candidate LTI-01 recently completed a phase 1b clinical trial in Australia and New Zealand for the treatment of loculated pleural effusions, a life-threatening condition associated with hospitalized pneumonia.

## Understanding IPF

Given its unique pipeline and world-leading scientific team, Lung Therapeutics has raised outside funding of $17 million, in addition to leveraging $27 million in research and development grants. In 2017, Lung Therapeutics successfully completed a $14.3 million series B financing round to support not only the development of LTI-01, but also its transformative fibrosis treatment, LTI-03.

"LTI-03 has a very unique and as yet unexploited mechanism of action that makes it very attractive for addressing and resolving fibrosis and fibrosis-related conditions," said Windsor. The company is focusing on its use in the treatment of IPF, a chronic lung disease in adults aged 65 years and over, which is characterized by progressive tissue scarring and is usually fatal within 3–5 years of diagnosis. Deaths are estimated at between 28,000 and 65,000 in Europe and between 13,000 and 17,000 in the United States[1]. Current drugs are unable to do more than slow the scarring process, and thus there is a real unmet need to improve clinical outcomes.

IPF is not fully understood, but there seems to be both a loss of healthy lung cells and the proliferation of unwanted fibrotic cells, believed to be caused in part by the dysregulation of biological signaling pathways.

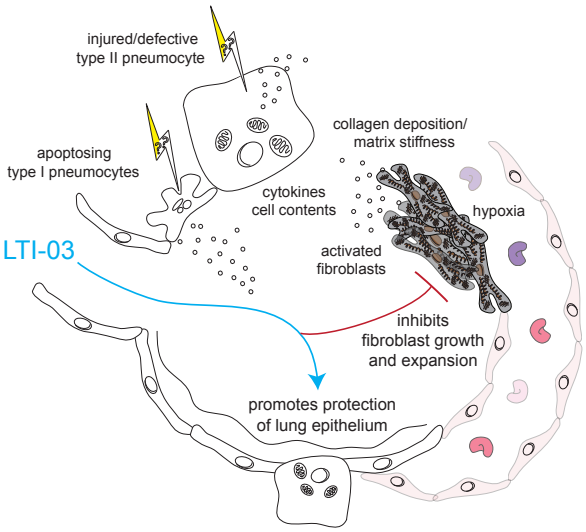


**Fig. 1 | Restoring cell balance with LTI-03.** Structural proteins are degraded and new proteins are formed.

Lung Therapeutics has focused on the pathway that produces caveolin 1 (Cav1). "In a fibrotic state the Cav1 protein is missing from fibroblasts whereas it would normally be present," said Windsor, "and caveolin seems to have a role in keeping fibrosis in check, so when you lose it, you lose this ability." Cav1 may in fact be important in many diseases caused by fibrosis.

## Targeting IPF with LTI-03

Lung Therapeutics new molecular entity, LTI-03, is a seven-amino-acid peptide, representing a portion of the caveolin scaffolding domain, a critical portion of Cav1. "We are adding something back to restore a balance in the cells that has gone awry," explained Windsor. By replacing the missing protein, the cells are able to promote normal extracellular matrix turnover—the process by which structural proteins such as collagens, elastin, and proteoglycans are degraded and new proteins are formed (**Fig. 1**). "Again if you lose caveolin you have lost the lungs' ability to remodel fibrosis and restore lung or organ function, so adding back the critical portion of the caveolin protein potentially could have far-reaching effects," Windsor added.

What is so exciting about this breakthrough is its potential to restore healthy function in patients. In animal studies, LTI-03 has been shown to resolve bleomycin or transforming growth factor-β-induced lung injury when given 14 days after the induction of injury. LTI-03 has also shown promise in other models of fibrotic diseases. "We have proof of concept in ten different models of fibrosis including two models of cardiac fibrosis, kidney fibrosis and scleroderma," said Windsor, "and every model system just gives us more information on the benefit of addressing this pathway in fibrosis. Lung Therapeutics is taking the lead in doing just that." The company anticipates the launch of phase 1 trials of LTI-03 for IPF in early 2019.

Key opinion leader Ganesh Raghu summarized the potential of LTI-03. "The need to improve outcomes for patients with IPF that are meaningful to patients confronted with IPF beyond the current standard of care persists. While the etiology of IPF is unknown, preventing injury/damage to the epithelium barrier and consequent expansion of fibroblast and extracellular matrix is an appropriate step in the right direction. In this regard, the drugs delivered to reach the epithelium in distal pulmonary parenchyma by inhalation are ideal as the disease is confined to the lung besides minimizing (if any) systemic effects/adverse reaction in the patient. LTI-03 has a great potential to accomplish this through unique signal transduction pathways. I look forward to continued research in developing the drug in an inhaled format for patients with IPF as it has the potential of improving outcomes for patients with IPF."

1. Hutchinson, J. P., McKeever, T. M., Fogarty, A. W., Navaratnam, V. & Hubbard, R. B. *Ann. Am. Thorac. Soc.* **11**, 1176–1185 (2014).

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