REIN Therapeutics

Harnessing fibrosis, unleashing life

Science Deck| September 2026

Forward Looking Statements

- This presentation and various remarks we make during this presentation contain forward-looking statements of Rein Therapeutics, Inc. (“Rein”, the “Company”, “we”, “our” or “us”) within the meaning of the Private Securities Litigation Reform Act of 1995, including statements with respect to: the expected benefits of using CSDs for fibrotic indications and our plans to develop and commercialize LTI-03, including the potential benefits thereof. We use words such as “anticipate,” ”believe,” “estimate,” “expect,” “hope,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “would,” “can,” “could,” “should,” “continue,” and other words and terms of similar meaning to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including (i) the risk that the Company may not be able to successfully continue its Phase 2 clinical trials of LTI-03; (ii) the risk that the Company may not report data derived from its Phase 2 trial in the second half of 2026 or, if it does, the risk that the data may not support or validate our expectations concerning the potential benefits of LTI-03; (iii) success in early phases of pre-clinical and clinical trials do not ensure later clinical trials will be successful; (iv) the risk that the Company’s present cash and cash equivalents may not be sufficient to fund the Company’s operations into the first quarter of 2028 and (v) the risks and uncertainties discussed in the “Risk Factors” section of the Company’s Annual Report on Form 10-K for the year ended December 31, 2025 filed with the Securities and Exchange Commission (the “SEC”) on March 2026 and in the subsequent filings that the Company files with the SEC. These forward-looking statements should not be relied upon as representing the Company's view as of any date subsequent to the date of this presentation, and we expressly disclaim any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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Outline

- Our story
- Introducing LTI-03 – a novel treatment for IPF
- Rationale for use of caveolin scaffolding domain peptides (CSDs) for fibrotic indications
- Background – CAV1 biology and fibrosis
- Lead selection and target validation
- LTI-03 formulation
- LTI-03 pharmacokinetics
- Translating efficacious dosing of LTI-03
- Evidence of alveolar restoration by LTI-03
- Evidence of anti-fibrotic effects of LTI-03 in preclinical fibrosis models
- Evidence of LTI-03 biomarker activity in Ph1b clinical trial (NCT05954988)
- Now enrolling RENEW Ph2 clinical trial (NCT06968845)

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Rein Therapeutics, Inc – Our Story

Pioneering First-in-Class Therapies for Pulmonary & Fibrosis Indications

- Clinical-stage biotech company **pioneering first-in-class multi-pathway therapies in orphan pulmonary and fibrosis indications**
- **LTI-03** has demonstrated antifibrotic and regenerative properties
  - **Unique dual mechanism** promoting alveolar epithelial cell survival & inhibiting profibrotic signaling
  - **No treatment-related SAEs** and no gastrointestinal tolerability signal over 14 days of inhaled dosing (n=24). Local lung delivery with minimal systemic exposure.

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Led by Experienced Biotech and Pulmonary Team

Key Management and Board of Directors

Brian Windsor, Ph.D.
Chief Executive Officer and Director

TFF, Enavail, Emergent

Cory H. Hogaboam, Ph.D.
Chief Scientific Officer

Cedars Sinai

Tim Cunningham
Chief Financial Officer

Danforth Advisors

Kristie Lauterbach
VP Quality

Takeda

Joe von Rickenbach
Chairman

Paraxel

Bill Fairey
Director

Myokardia, ChemoCentryx
Actelion

Alan Musso
Director

Reviral, Peloton, Targacept

Reinhard Ambros, Ph.D.
Director

Funded by Novartis

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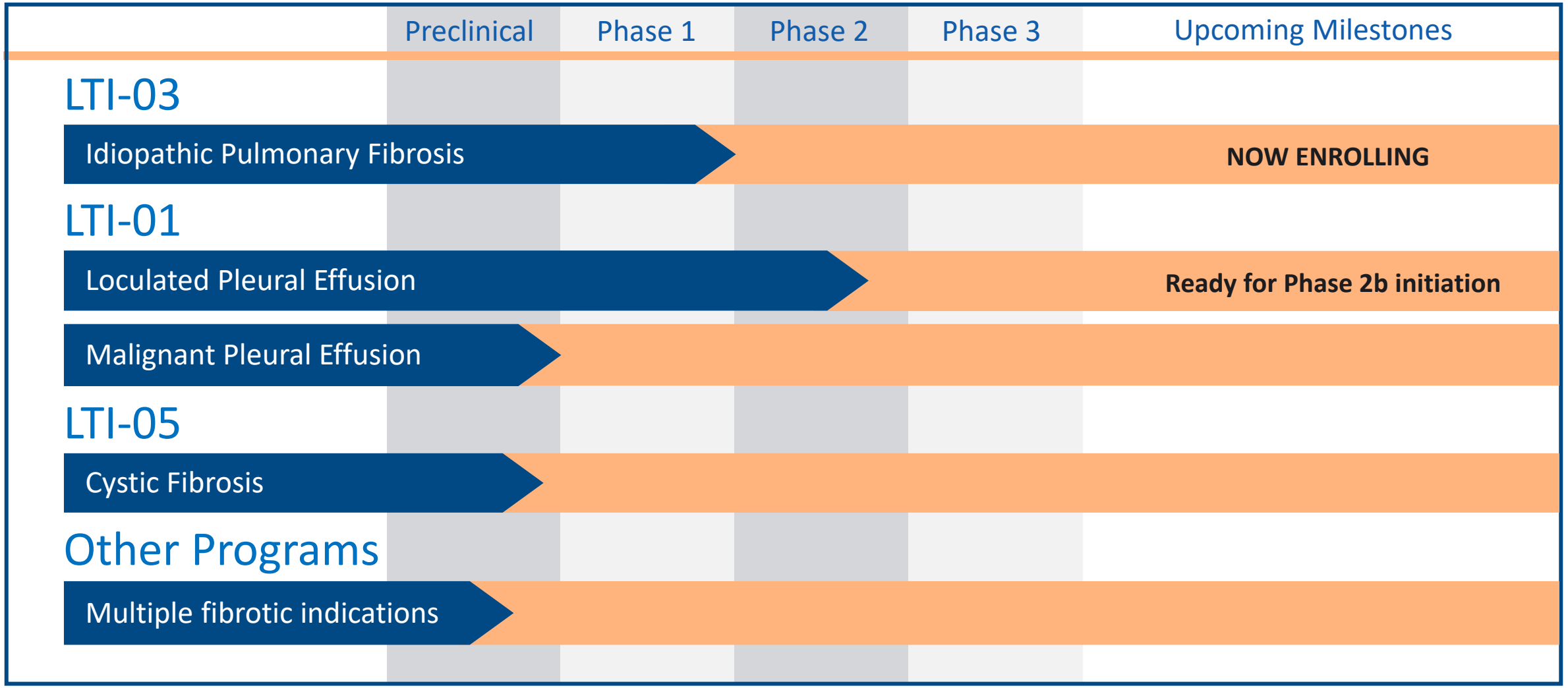
Multiple Orphan Disease Programs Ready for Phase 2 Clinical Trials



Therapies for Underserved Fibrosis and Pulmonary Conditions

LTI-03 ***Idiopathic Pulmonary Fibrosis***	***Advancing into Phase 2***	• Phase 1b clinical trial met primary endpoint: High dose LTI-03 (10mg) and low dose LTI-03 (5mg) was **well-tolerated**; **no treatment-related SAEs.** • Exploratory biomarkers previously associated in the literature with lung function decline were directionally consistent with preclinical findings; **5 biomarkers reached nominal significance at the higher dose; 2 in the lower dose**
LTI-01 ***Loculated Pleural Effusions***	***Phase 2b ready***	• **Potentially fatal disease** with **no approved drugs** • Completed Phase 1b and Phase 2 trials; similar mechanism as existing, off label therapeutic use

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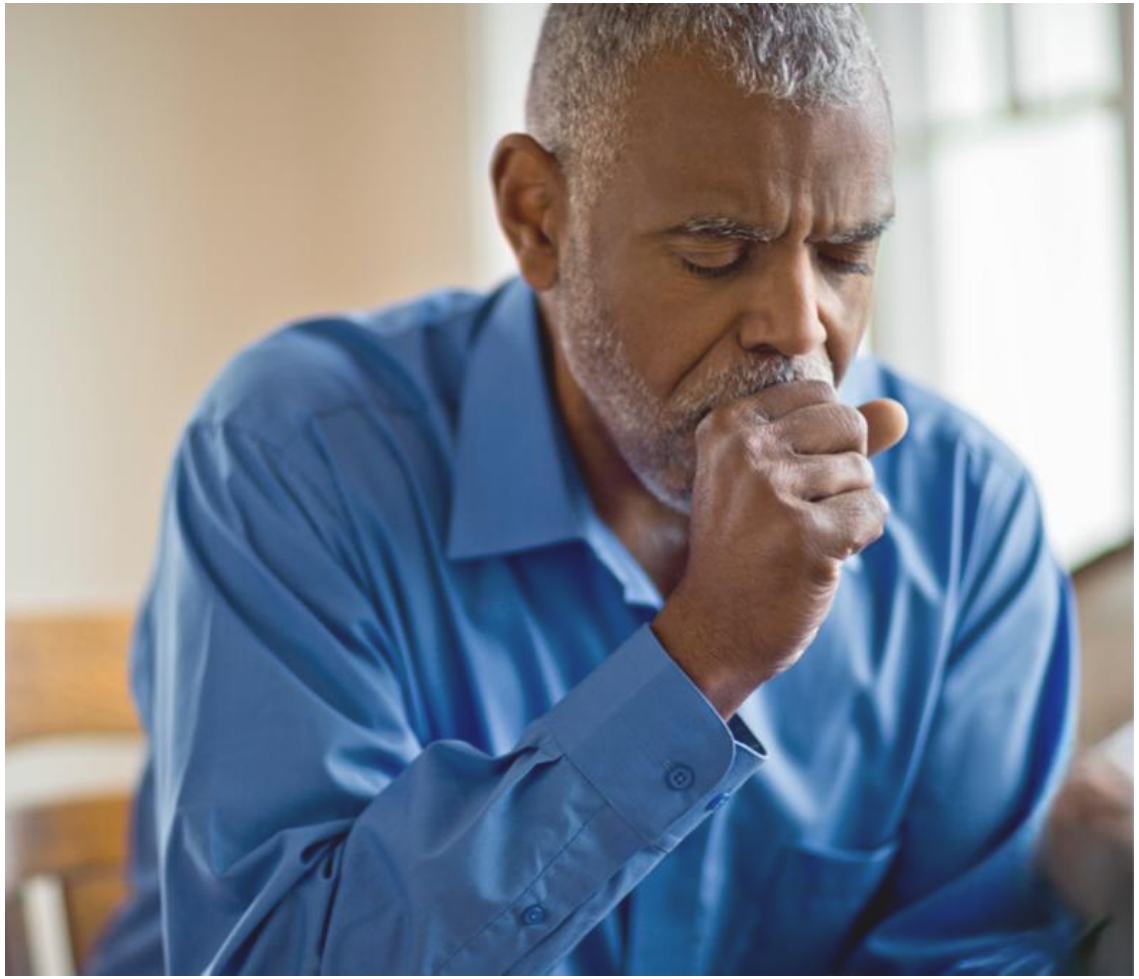
LTI-03: A Novel Treatment with Potential to Reverse the Course of IPF

Idiopathic Pulmonary Fibrosis – a Deadly Diagnosis

- Idiopathic Pulmonary Fibrosis, or IPF, is a fatal age-related disease characterized by progressive scarring in the lungs[1]
- IPF is part of a larger group of diseases known as Interstitial Lung Diseases, or ILDs, which are diseases characterized by lung inflammation and/or scarring. There are more than 200 types of Pulmonary Fibrosis conditions within ILDs[2]
- Estimated US prevalence is 14 to 43 per 100,000; approximately 40,000 to 110,000 adults live with IPF.[3]
- More than 250,000 Americans live with some form of pulmonary fibrosis.[2]
- Median survival from the time of diagnosis is 3-5 years [4]



[1]Mora, A., Rojas, M., Pardo, A. et al. Emerging therapies for idiopathic pulmonary fibrosis, a progressive age-related disease. Nat Rev Drug Discov 16, 755–772 (2017).
[2] https://www.pulmonaryfibrosis.org/understanding-pff/about-pulmonary-fibrosis/what-is-pulmonary-fibrosis
[3] Raghu G, Weycker D, Edelsberg J, Bradford WZ, Oster G. Incidence and prevalence of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2006;174(7):810–816. doi:10.1164/rccm.200602-163OC
[4]Ley B, Collard HR, King TE Jr. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2011;183(4):431–440.

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Sizable Global Opportunity with Potential Upside

- Three drugs approved for IPF as of September 2026 (nintedanib, pirfenidone, nerandomilast)
- Ofev®, the global leader, did more than $4B in sales.
- Other PF and ILDs represent upside for a successful IPF drug

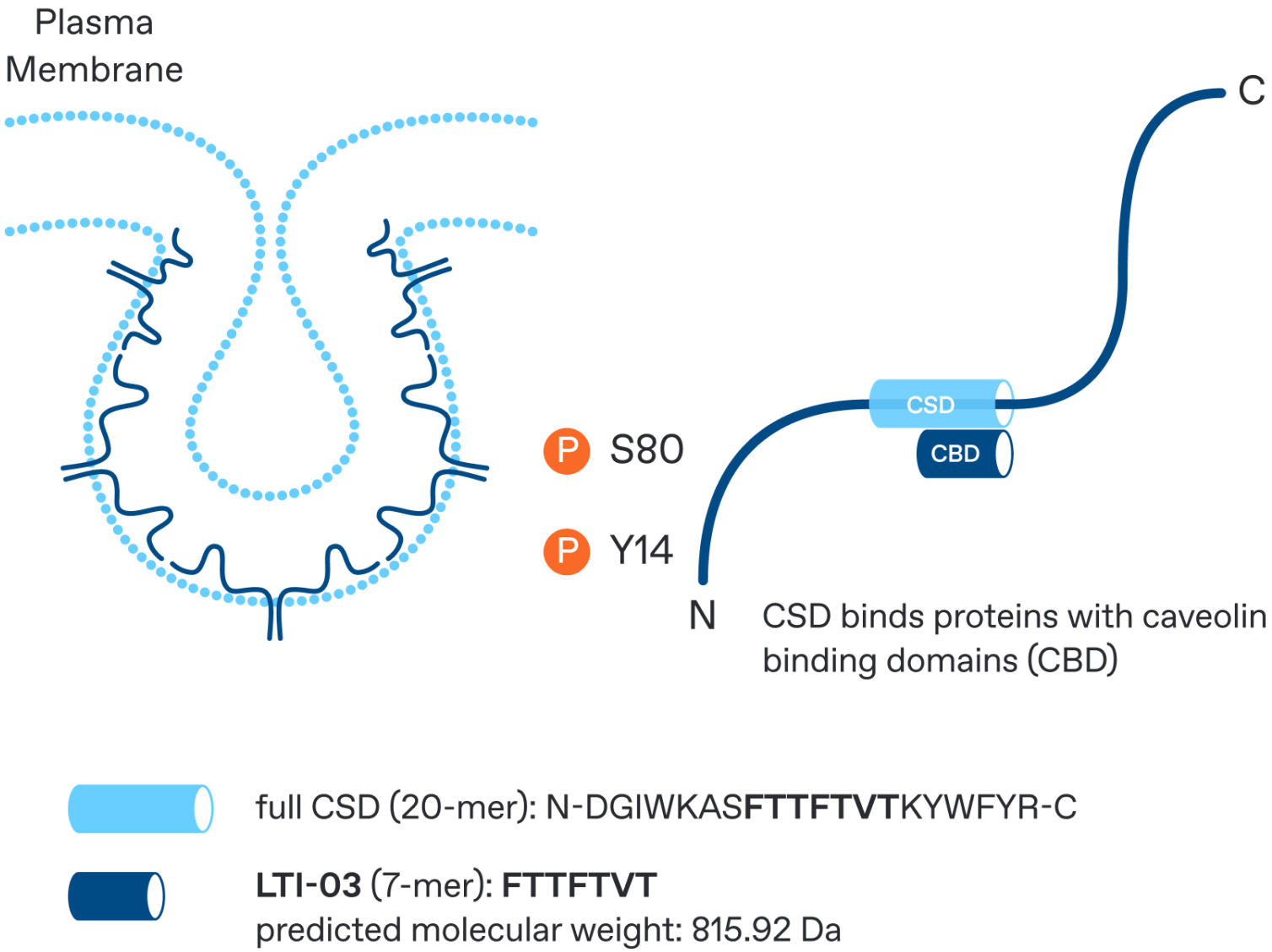
Select Competitive Landscape[1]

Company	Compound	Single or Multi-pathway	Mechanism	Target Cell Types	Clinical Stage
REIN TX	LTI-03	Multi-pathway	Caveolin-1 CSD mimic	Fibroblasts, type 2 Epithelial cells, Aberrant basaloid cells, Macrophages	ENROLLING
Boehringer Ingelheim	Nintedanib	Multi-pathway	Broad tyrosine kinase inhibitor	Fibroblasts	Approved
Roche	Pirfenidone	Multi-pathway	unknown	Fibroblasts	Approved
Boehringer Ingelheim	Nerandomilast	Multi-pathway	PDE-4B inhibitor	Aberrant basaloid cells, Fibroblasts	Approved
ENDEAVOR BioMedicines	ENV 101	Single	Smoothened antagonist	Fibroblasts	P2
vicore pharma	Buloxibutid	Single	Angiotensin II type 2 receptor agonist	Type 2 Epithelium	P2b
avalyn pharma	AP02	Multi-pathway	Broad tyrosine kinase inhibitor	Fibroblasts	P2
Celea THERAPEUTICS	Deupirfenidone	Multi-pathway	unknown	Fibroblasts	P3

Rationale for administration of caveolin scaffolding domain peptides (CSDs) as therapeutics for fibrotic indications

LTI-03: the Critical Portion of the CSD Region of Cav1
Mimics the Regulatory Activity of Cav1, Affecting a Wide Range of Proteins Involved in Fibrosis

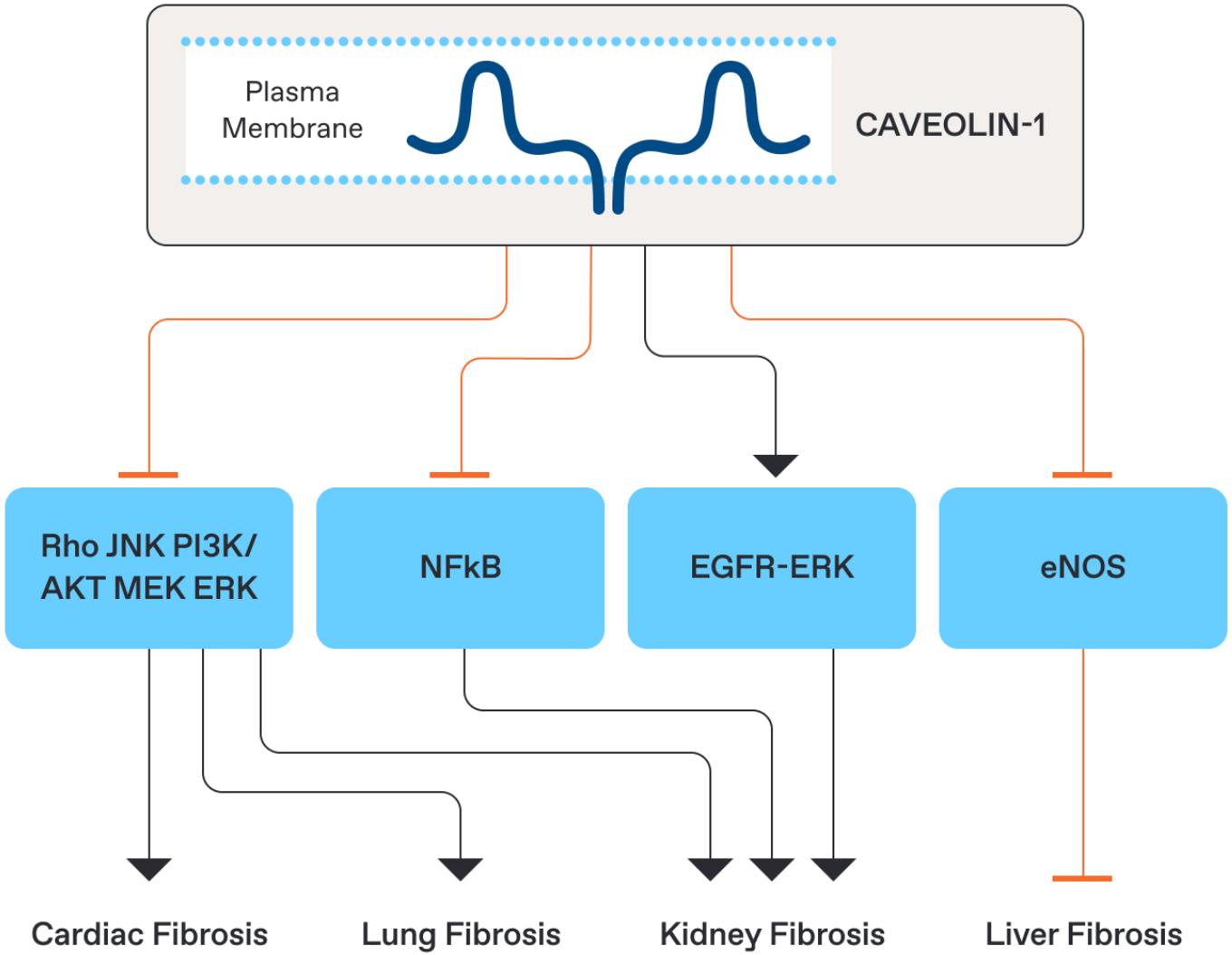
- LTI-03 is a seven amino acid peptide comprising a portion of the Cav1 CSD. Substitution/deletion analysis revealed it is the smallest CSD fragment that retains functionality
- This hydrophobic peptide can enter cells, and it may be acting both at the cell membrane and intracellularly
- Studies have shown that the LTI-03 peptide can affect phosphorylation of dozens of profibrotic proteins
- LTI-03 is dosed direct to the lungs by dry powder inhaler, and studies have shown that intact peptide can be detected in the lungs 24 hours after administration



For a review on CSD/CBD binding domain list, see: Byrne et. al. PLOS One 2012

Caveolin-1 Regulates Proteins Involved in Multiple Fibrosis-Related Pathways in the Lung and Other Organs

- Caveolin-1 (Cav1) is a regulator of cellular homeostasis
- Cav1 regulates many proteins involved in **multiple fibrosis pathways**
- Cav1 effects its regulation through interacting at the **Caveolin Scaffolding Domain (CSD)**, a 20 amino acid region that binds proteins and affects trafficking through phosphorylation
- Cav1 is lost in a fibrotic state—it is dramatically downregulated both at the transcript and protein level and thus loses its ability to properly regulate proteins involved in fibrosis[1]
- This is not limited to the lung. Cav1 is involved in fibrosis in the heart, skin, kidney, liver, and other organs

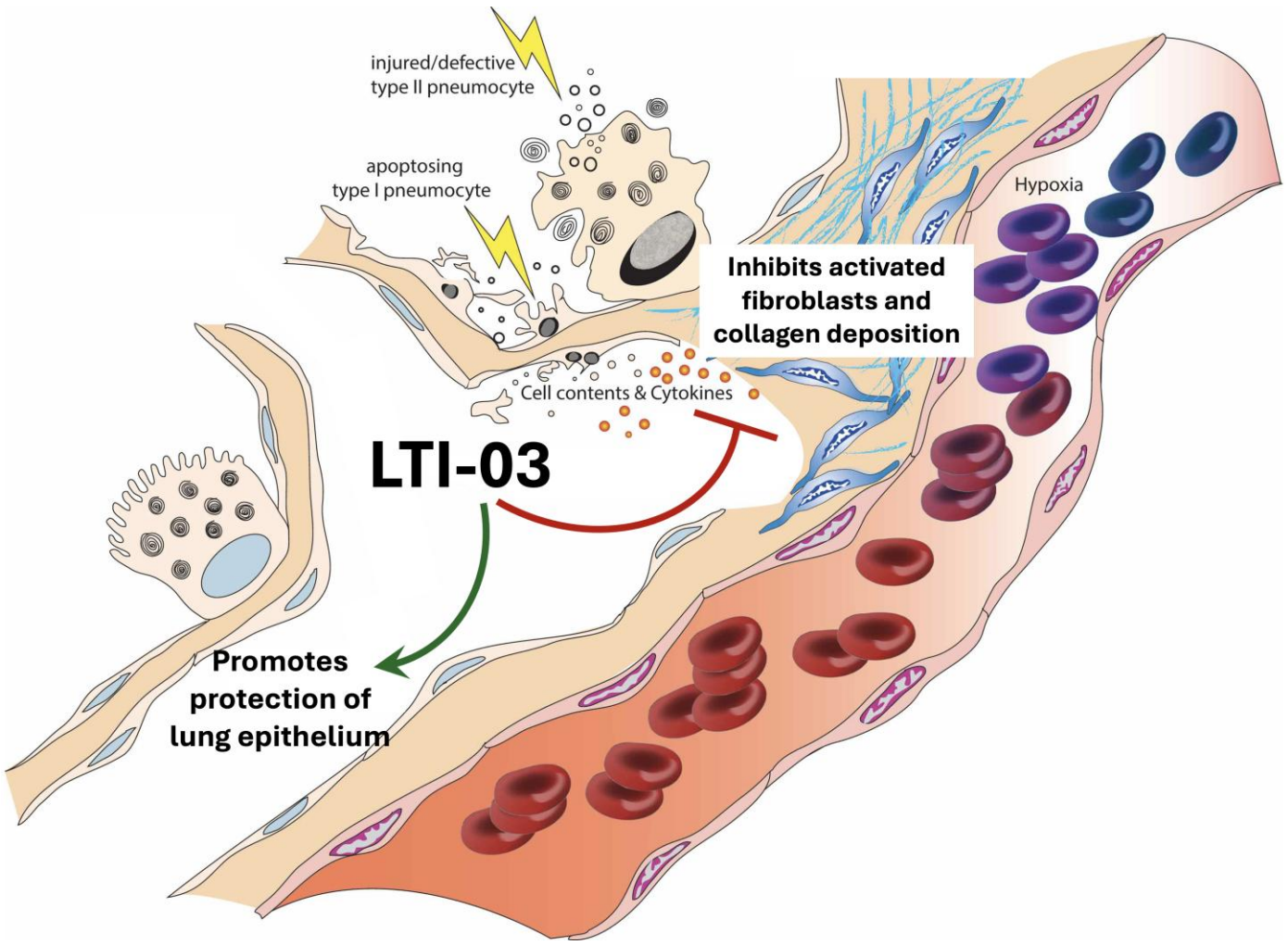


Adapted from Gvaramia et al, Matrix Biology, 2013

[1]Wang XM et al. Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis. J Exp Med. 2006 Dec 25;203(13):2895-906.

LTI-03's Dual Mechanism: Broad Antifibrotic Activity Combined with Epithelial Protection

- Approved therapies slow the rate of lung function decline but do not restore lung function
- LTI-03 inhibits profibrotic signaling and supports alveolar epithelial cells by replacing caveolin-1 scaffolding domain activity lost in the IPF lung
- LTI-03 works to impact multiple fibrosis pathways
- LTI-03 has attenuated fibrosis in preclinical cardiac and dermal models, suggesting potential beyond the lung

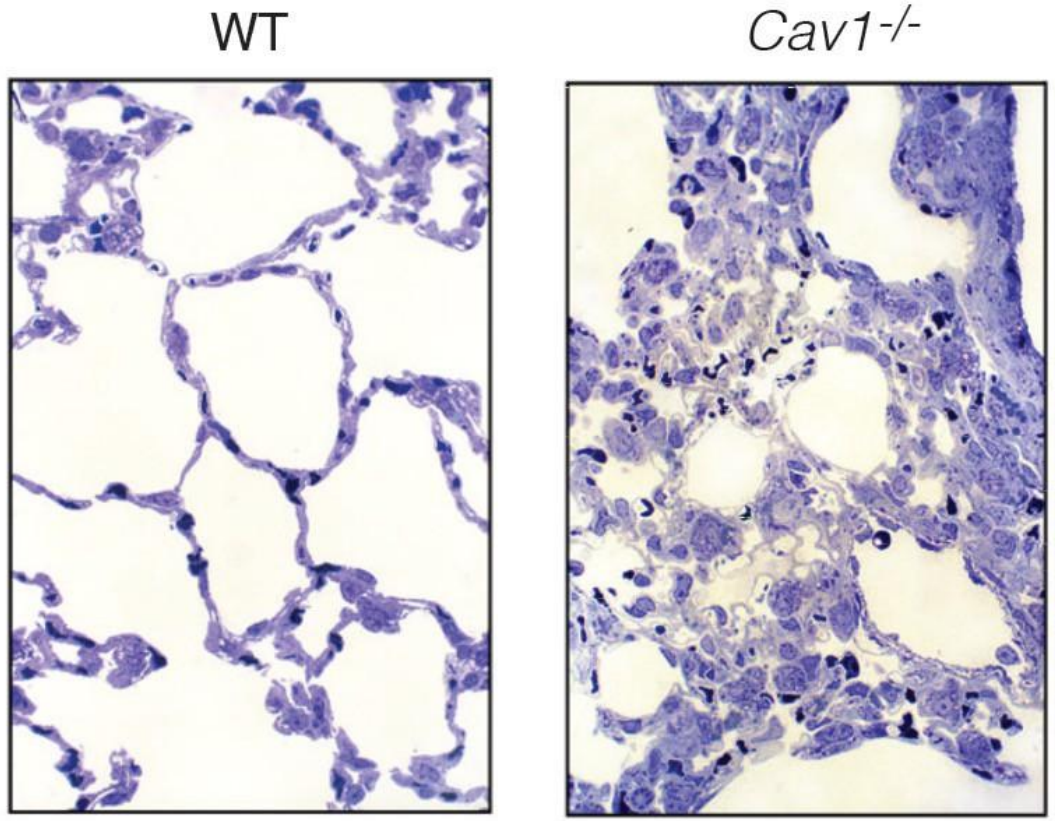


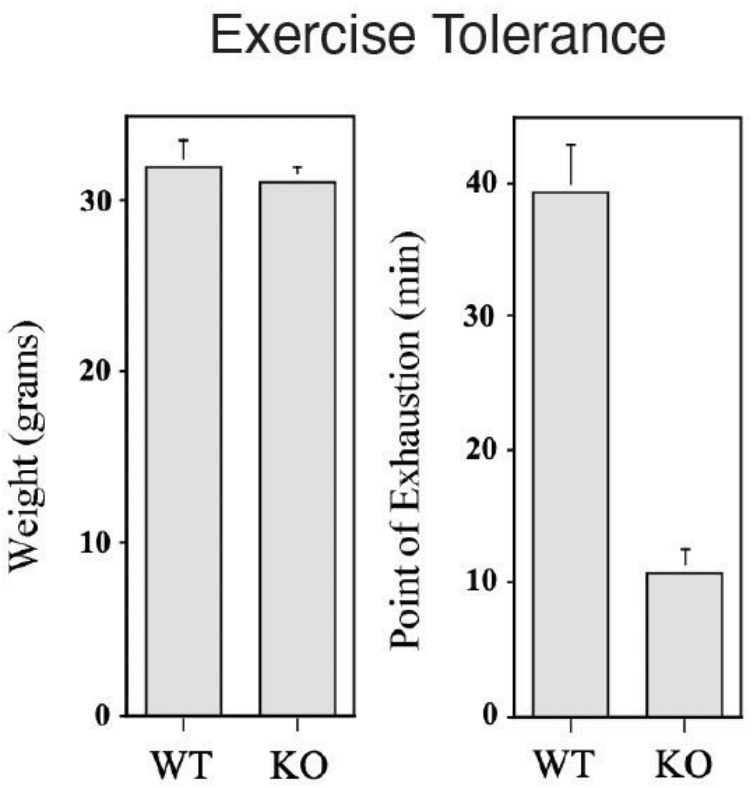
Background

CAV1 biology and fibrosis

CSD peptides guide cells towards homeostasis

Caveolin-1 mouse knockouts develop thickened lung septa and display reduced exercise tolerance due to lung defects





One-µm sections of lung parenchyma were cut and stained with toluidine blue. Cav1-deficient mice displayed significantly smaller, constricted, alveolar spaces with thickened alveolar septa and hypercellularity. In addition, an intolerance to exercise (failure to maintain buoyancy while swimming) was noted likely due to lung defects as weight was similar to wild type [6].

SOURCE: Razani et. al. J BIOL CHEM 2001

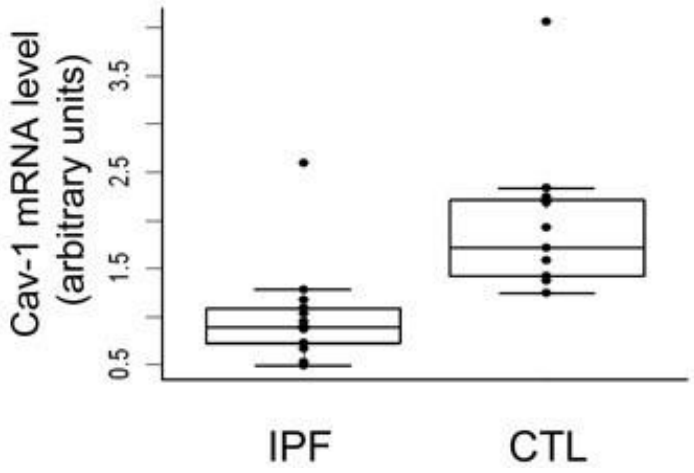
Rockefeller University Press

Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis

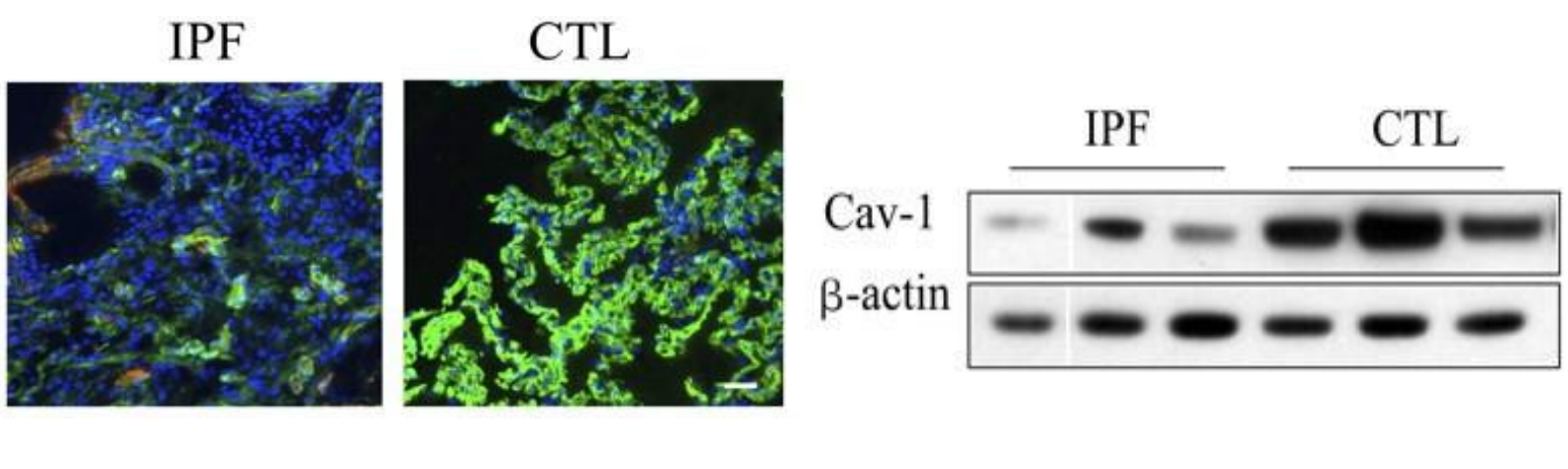
JEM Journal of Experimental Medicine

Xiao Mei Wang,[1] Yingze Zhang,[1] Hong Pyo Kim,[1] Zhihong Zhou,[1] Carol A. Feghali-Bostwick,[1] Fang Liu,[1] Emeka Ifedigbo,[1] Xiaohui Xu,[2] Tim D. Oury,[3] Naftali Kaminski,[1] and Augustine M.K. Choi[1]

Caveolin-1 is downregulated in IPF



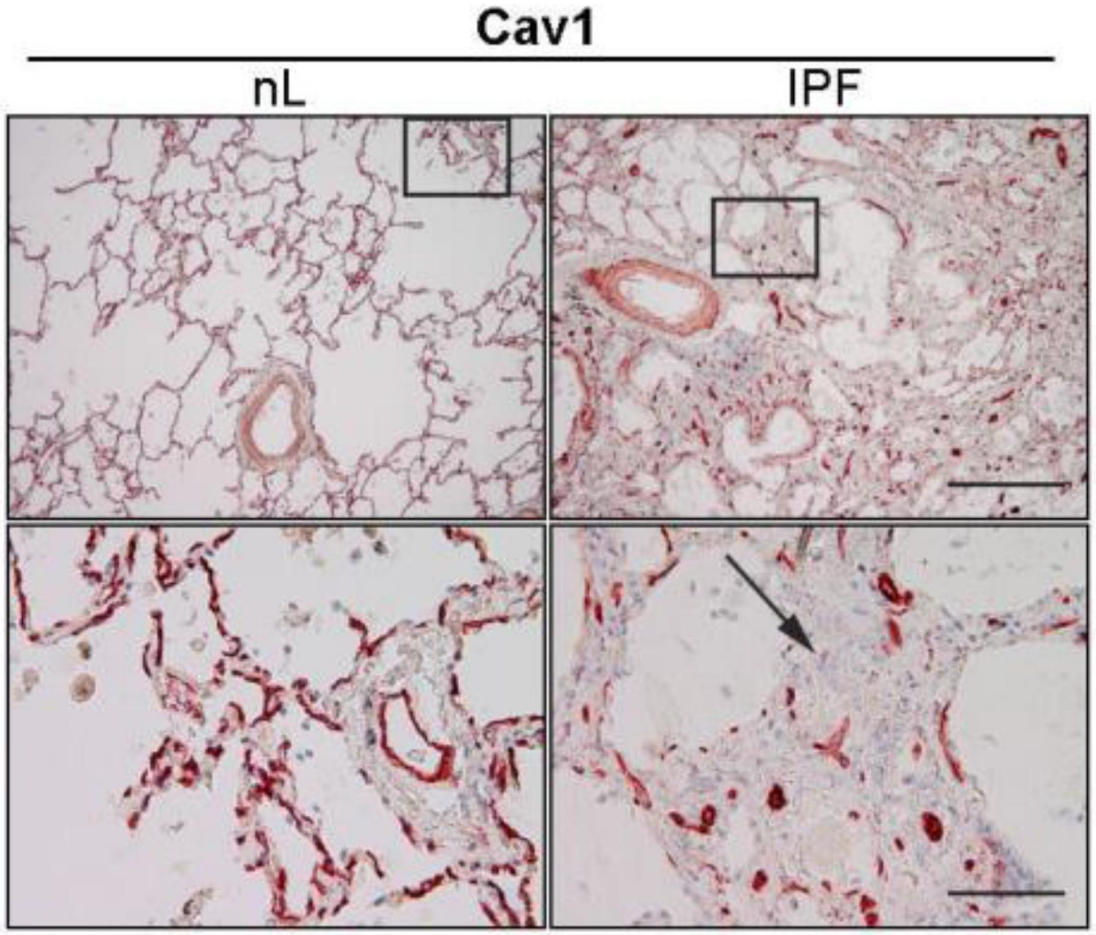
mRNA levels



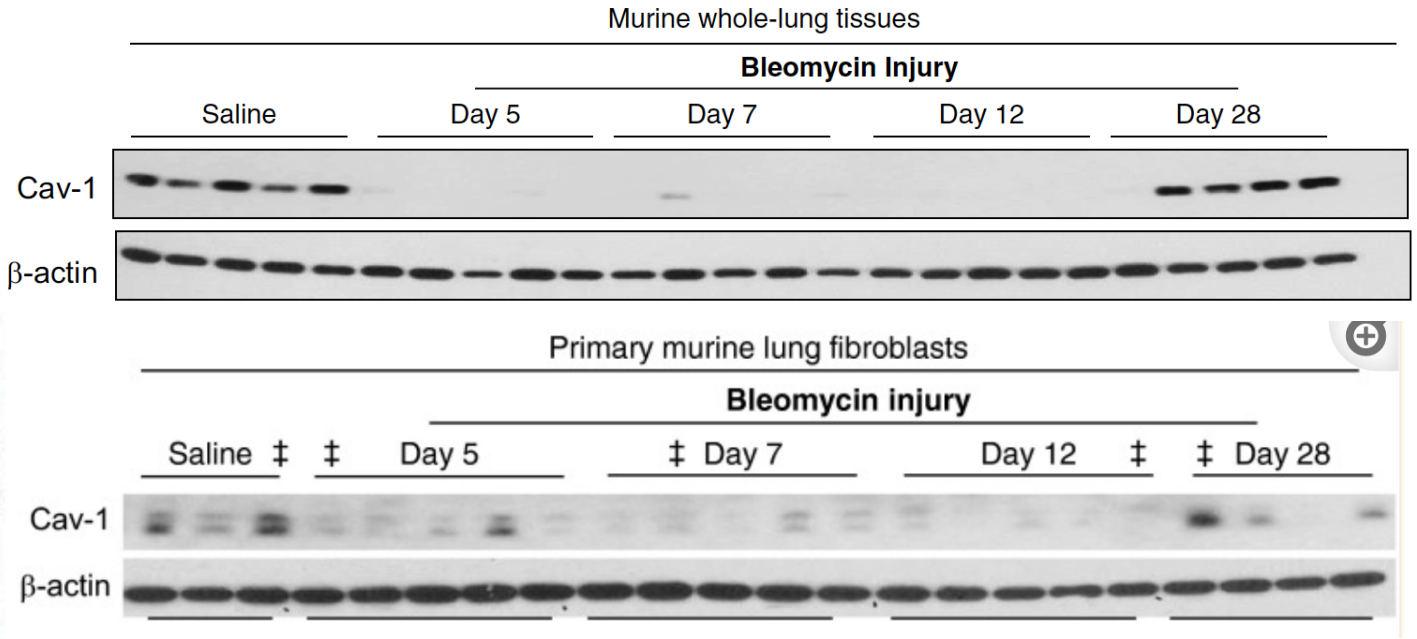
Protein expression

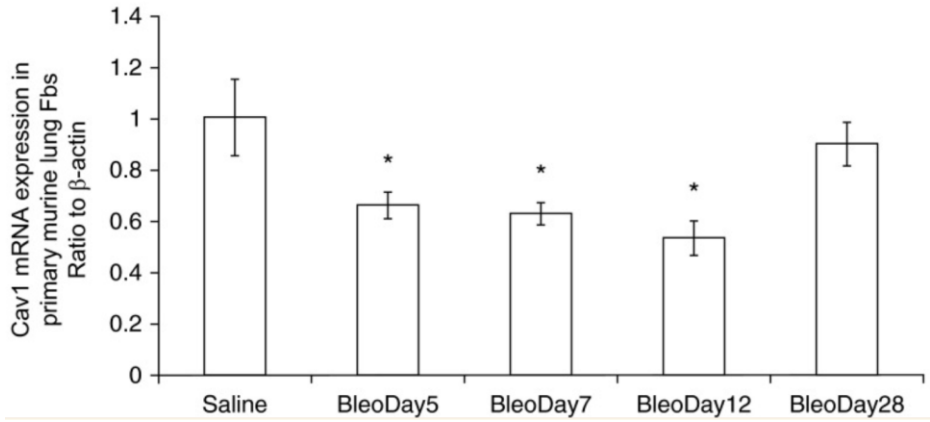
SOURCE: Wang XM, Zhang Y, Kim HP, et al. Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis. J Exp Med. 2006;203(13):2895-2906. doi:10.1084/jem.20061536.

Endogenous Caveolin-1 is depleted in end stage IPF lungs & during BLM injury



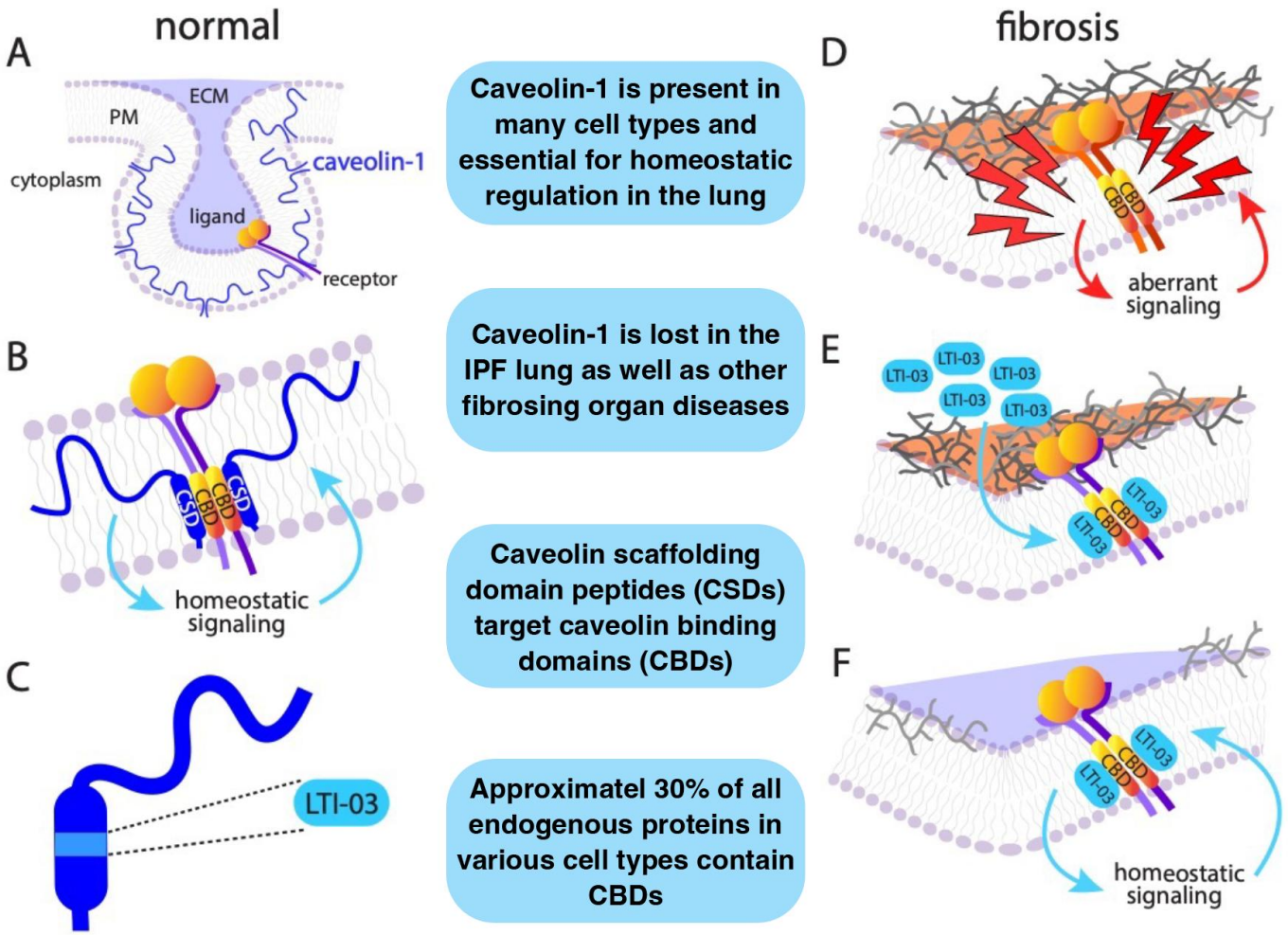
- *Nagaraja et al., Am J Path Sept 2018, UT Tyler*





Sanders et al., Am J Respir Cell Mol Biol. 2017

CAV1 signaling is lost in fibrosis and CSD peptides guide cells of fibrotic tissues towards homeostasis



Caveolin-1 is present in many cell types and essential for homeostatic regulation in the lung

Caveolin-1 is lost in the IPF lung as well as other fibrosing organ diseases

Caveolin scaffolding domain peptides (CSDs) target caveolin binding domains (CBDs)

Approximatel 30% of all endogenous proteins in various cell types contain CBDs

iScience

CellPress
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Article

LTI-03 peptide demonstrates anti-fibrotic activity in *ex vivo* lung slices from patients with IPF

BreAnne MacKenzie,[1,9,10,*] Poornima Mahavadi,[2,9,*] Yago Amigo Pinho Jannini-Sa,[3,9,*] Brecht Creyns,[3,9] Ana Lucia Coelho,[3] Milena Espindola,[3] Clemens Ruppert,[2] Brian Windsor,[1] Clemens Aigner,[4] Cory M. Hogaboam,[3] and Andreas Guenther[2,5,6,7,8]

Lead Selection and Validation

Screening for levels of fibrotic mediators in IPF fibroblasts with CSD truncations, substitutions and deletions led to selection of LTI-03; RPPA assay revealed broad anti-fibrotic activity

Lead selection

In a human IPF lung fibroblast screen for pro-fibrotic proteins, 7-mer (LTI-03) demonstrated maximum efficacy in attenuation of pro-fibrotic factors

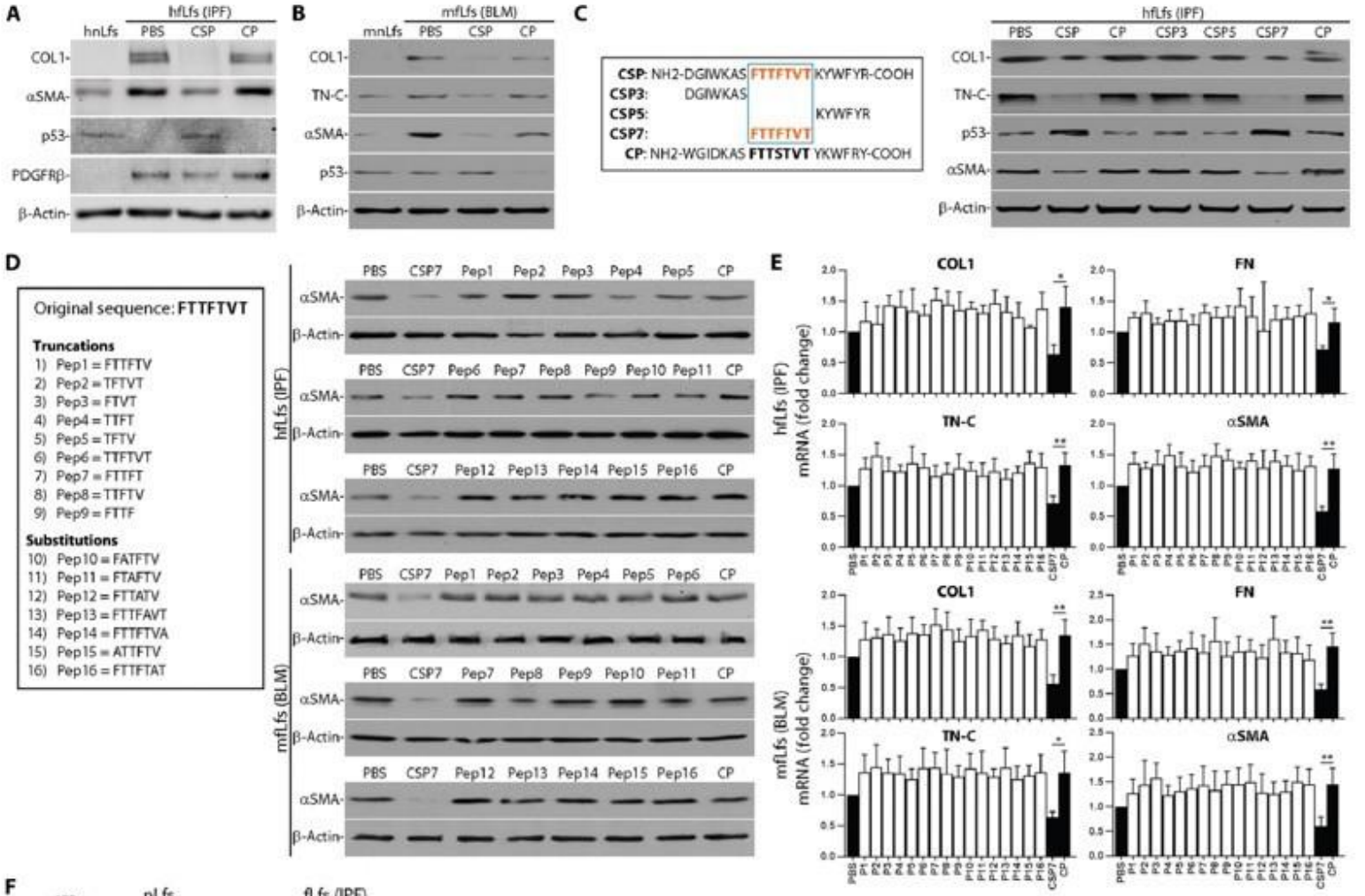


Fig. 1. Suppression of profibrogenic responses in fLfs by CSP or its deletion peptides. (**A**) Human non-fLfs (hnLfs) and hfLfs (hfLfs) isolated from the lung tissues of healthy donors and patients with IPF or (**B**) mouse non-fLfs (mnLfs) and mouse fLfs (mfLfs) from uninjured mice and mice with BLM-induced PF, respectively, were treated with PBS, CSP (10 μM), or CP for 48 hours. Conditioned media and cell lysates were immunoblotted. (**C**) A series of overlapping deletions were made in CSP, and hfLfs were treated with these peptides and assessed for p53 and profibrogenic proteins to identify the minimum amino acids required for the CSP effects. (**D**) A series of truncations/mutations were made in CSP7 and tested in hfLfs and mfLfs using αSMA expression to assess bioactivity. (**E**) Total RNA from hfLfs and mfLfs treated with CSP7 or truncated or mutated CSP7 were analyzed for COL1, αSMA, FN, and TN-C mRNA by qRT-PCR. The values are presented as bar graphs after normalization with β-actin transcript. (**F**) hnLfs and hfLfs treated with PBS, CSP7, or CP for 48 hours were subjected to MTT assay to assess proliferation. The experiments were repeated two (A to D) or three times (E and F). Data in (E) and (F) are represented as means ± SD. $^{*}P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$ were obtained by one-way analysis of variance (ANOVA) with Turkey's multiple comparison test.

SOURCE: Marudamuthu AS, Bhandary YP, Fan L, et al. Caveolin-1-derived peptide limits development of pulmonary fibrosis. Sci Transl Med. 2019;11:eaat2848. doi:10.1126/scitranslmed.aat2848.

Reverse phase protein array (RPPA) indicates that 10uM LTI-03 significantly attenuates a variety of profibrotic signaling pathways in IPF lung fibroblasts

A

Receptor tyrosine kinases and associated signaling

Antibody target protein	p-value
ALK(D5F3)	*
p-ALK(3B4)(Y1586)	***
c-Jun	*
p-c-Myc(T58)	**
Herb2/ErbB3	***
p-EGFR(Y1173)(53A5)	***
p-MEK (1/2)	****
p44/42 MAPK (ERK1/2)	*
p-PDK1(S241)	****
p-PDGFRβ (Y751)	****
p-RafB(S445)	****
p-Ret(Y905)	**
Stat5a	*
p-Stat5(Y694)	***
PI3Kp110a	**
p-SRC	****
SRC-1	***
YAP	**

Metabolic signaling

AMPKa	****
p-AMPKa1 (S485)	****
p-AMPKb1(S108)	****
Deptor	**
LDHA	**
p-mTOR	****
p-Raptor	****
PFKFB3	**
Raptor	**
p-Tuberin	****

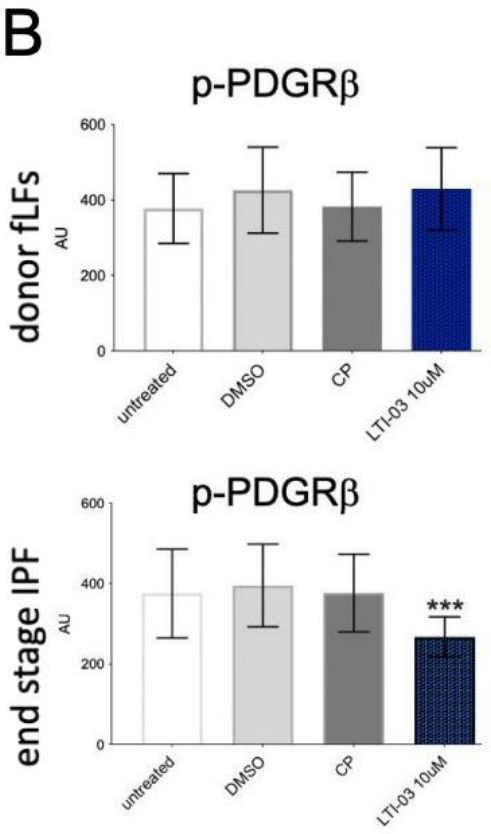
Invasion associated markers

TWIST2	*
Wnt5ab	**

HDACs

HDAC4	*
HDAC6	***

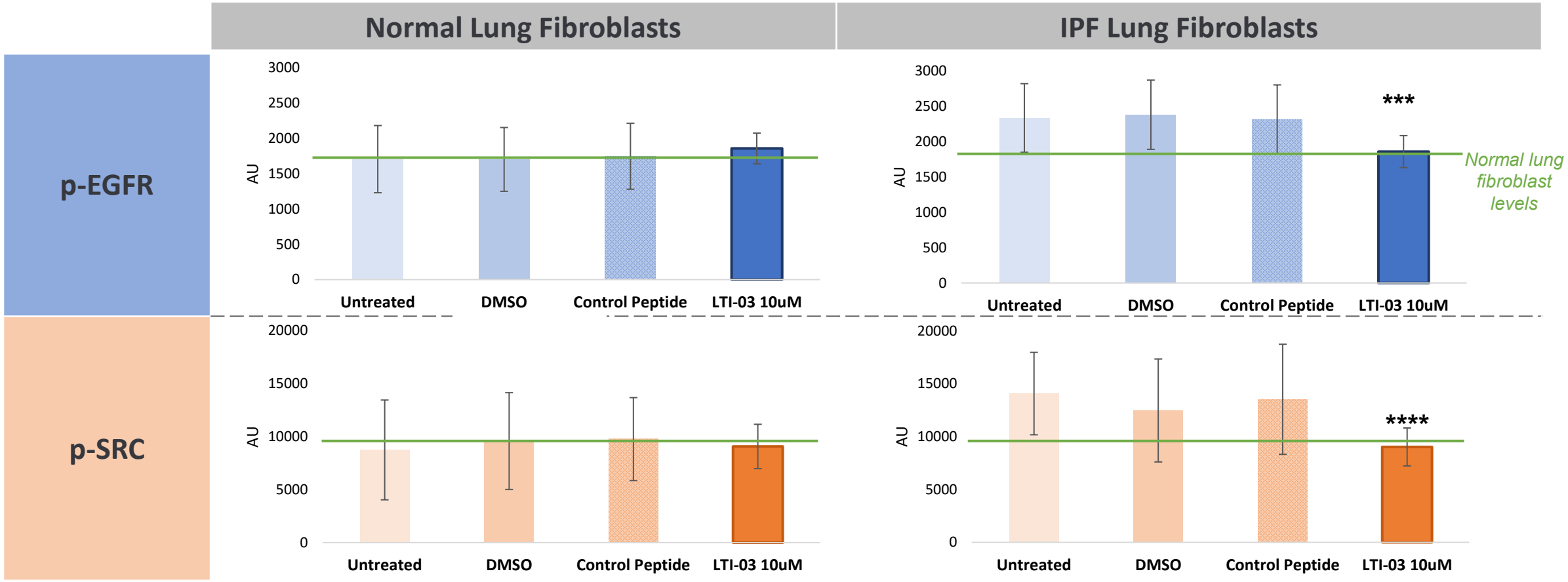
B



Panel A: RPPA assay results indicated significant reduction in many receptor tyrosine signaling factors, metabolic signaling factors, invasion associated markers and histone deacetylases.
Panel B: A representative graph illustrating that compared to untreated, DMSO control or control peptide (CP) , LTI-03 significantly attenuated p-PDGFRβ in IPF fibroblasts but had no effect on donor lung fibroblasts.
Data expressed as mean values and SDs. ,*$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ following one-way ANOVA and Bonferroni multiple comparison test.

*RPPA assay, biologically unique IPF lung fibroblasts (N=3) and donor lung fibroblasts (N=3); Shixia Huang; Baylor College of Medicine; Note(s) Data expressed as mean values and SDs. *p < .05; ** p < .01; ***p<001.; ****p < .0001 (DATA UNPUBLISHED)*

LTI-03 Attenuates Profibrotic Signaling in Vitro



- Factors indicative of aberrant profibrotic signaling were significantly **down-regulated exclusively in fibroblasts derived from IPF patients (n=3),** with little to no effects on healthy donor fibroblast lines (n=3); (LTI-03 10uM compared to untreated, DMSO or control peptide)
- In IPF, LTI-03 appears to **reduce aberrant signaling** by **supplementing cells with the Cav1 signaling domain**

*RPPA assay, Shixia Huang; Baylor College of Medicine; Note(s) Data expressed as mean values and SDs. *p < .05; ** p < .01; ***p<.001; ****p < .0001 (DATA UNPUBLISHED)*

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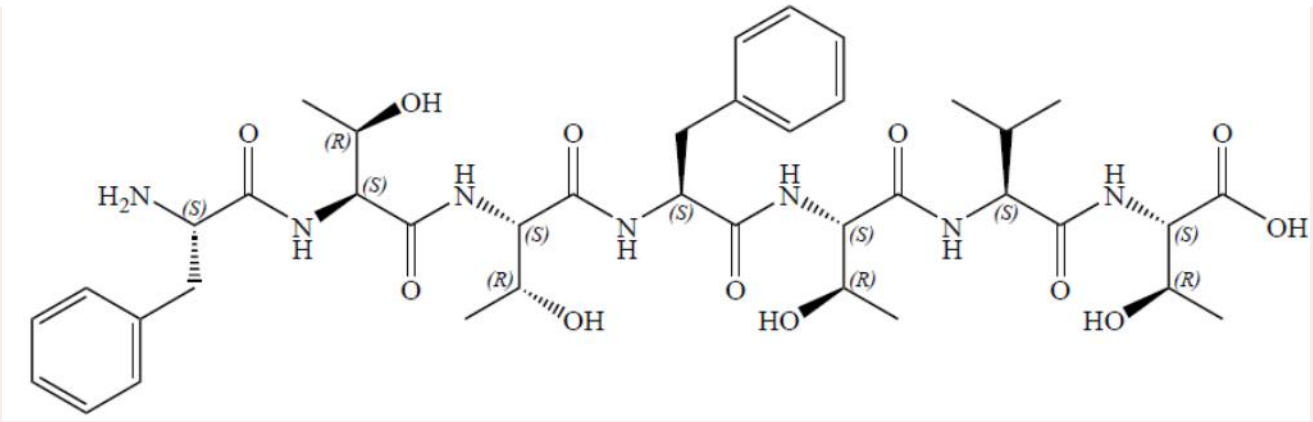
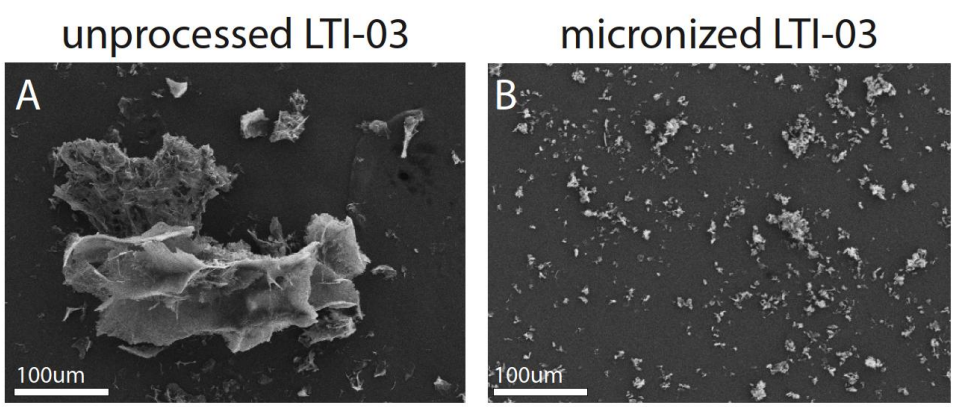
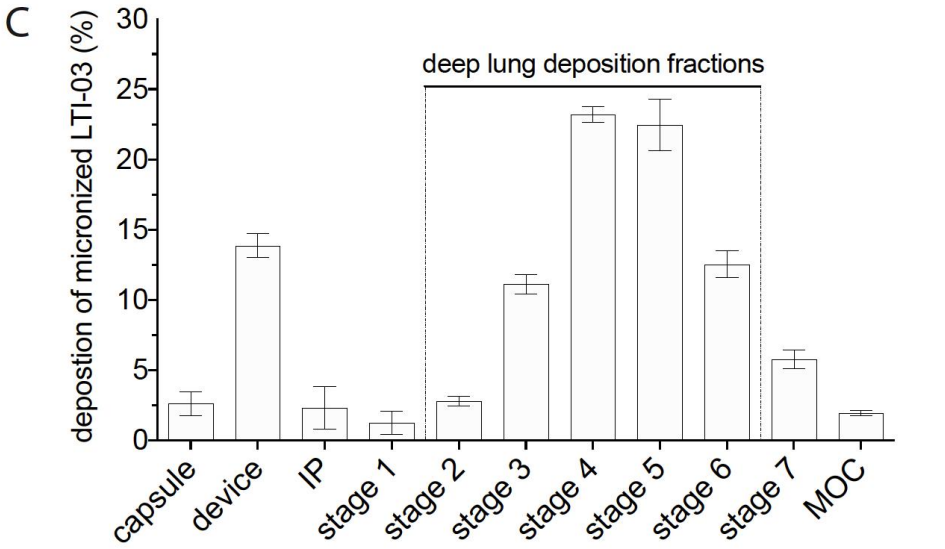


LTI-03 formulation

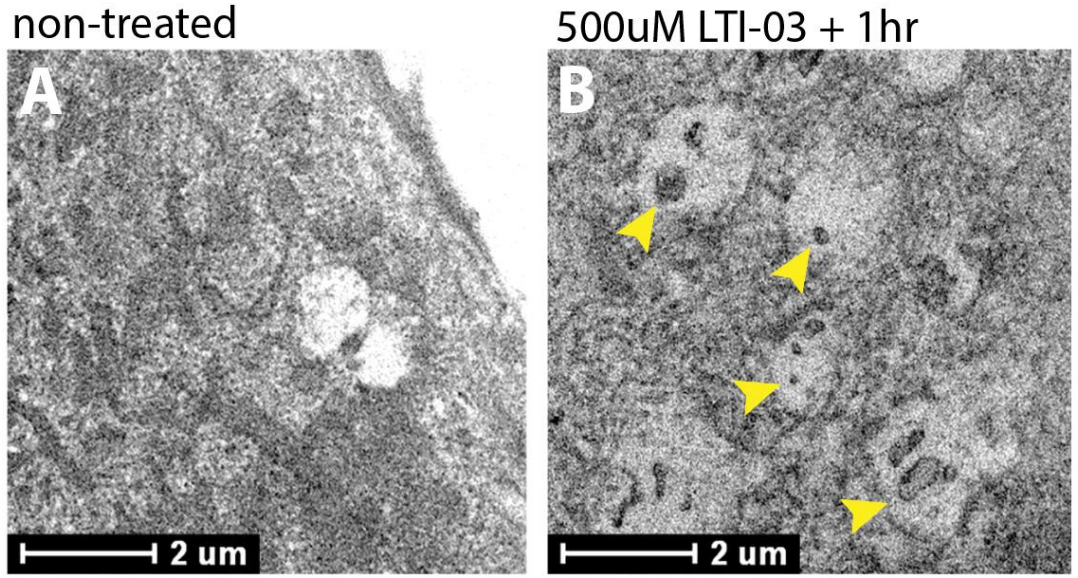
Dry powder: LTI-03 (7-mer) Indication: IPF (excipient free dry powder)

LTI-03 is a novel, excipient-free, stable, dry powder peptide

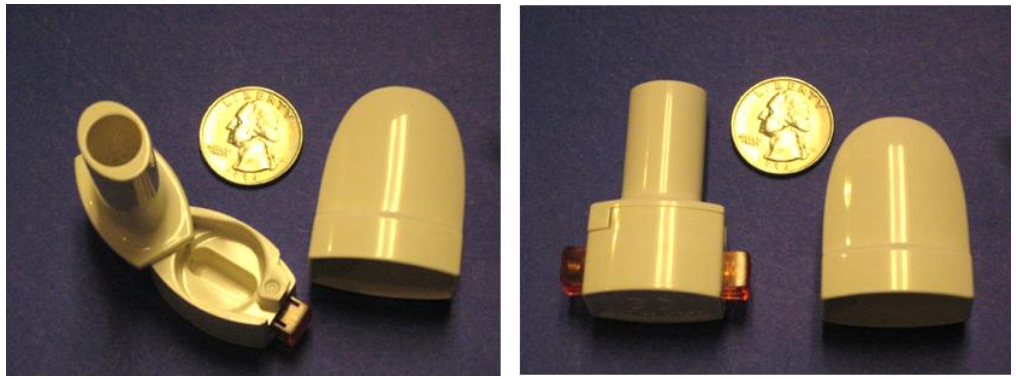




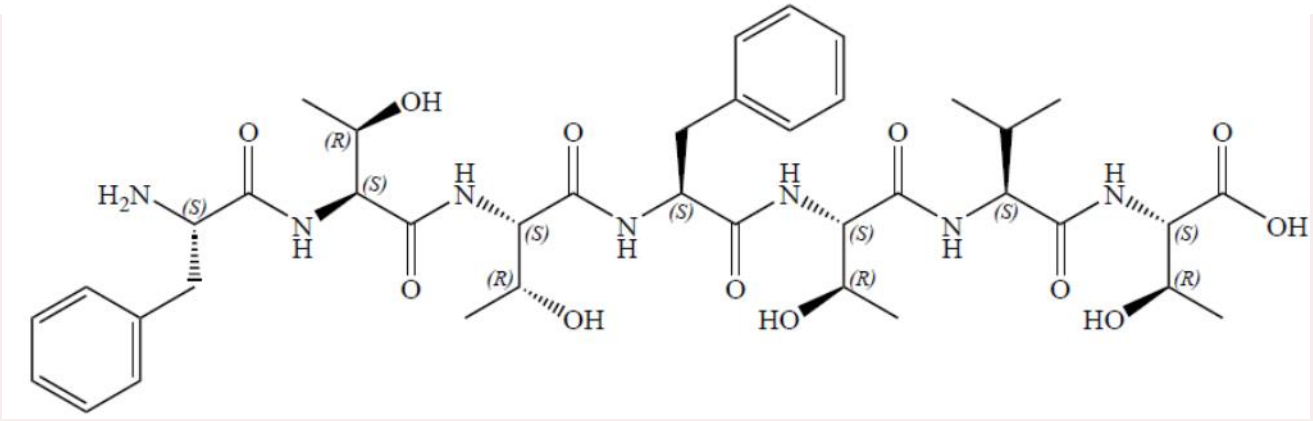
Batch 181028	Flow Rate	FPF% (<5 µm)	EF%	MMAD (µm)	GSD
Initiate	60 L/min	93.3 ± 3.3%	83.5 ± 0.1	1.58 ± 0.10	1.91 ± 0.03



- TEM microscopy indicates micronized LTI-03 is taken up by cells (fibroblasts) post 15min incubation (above)

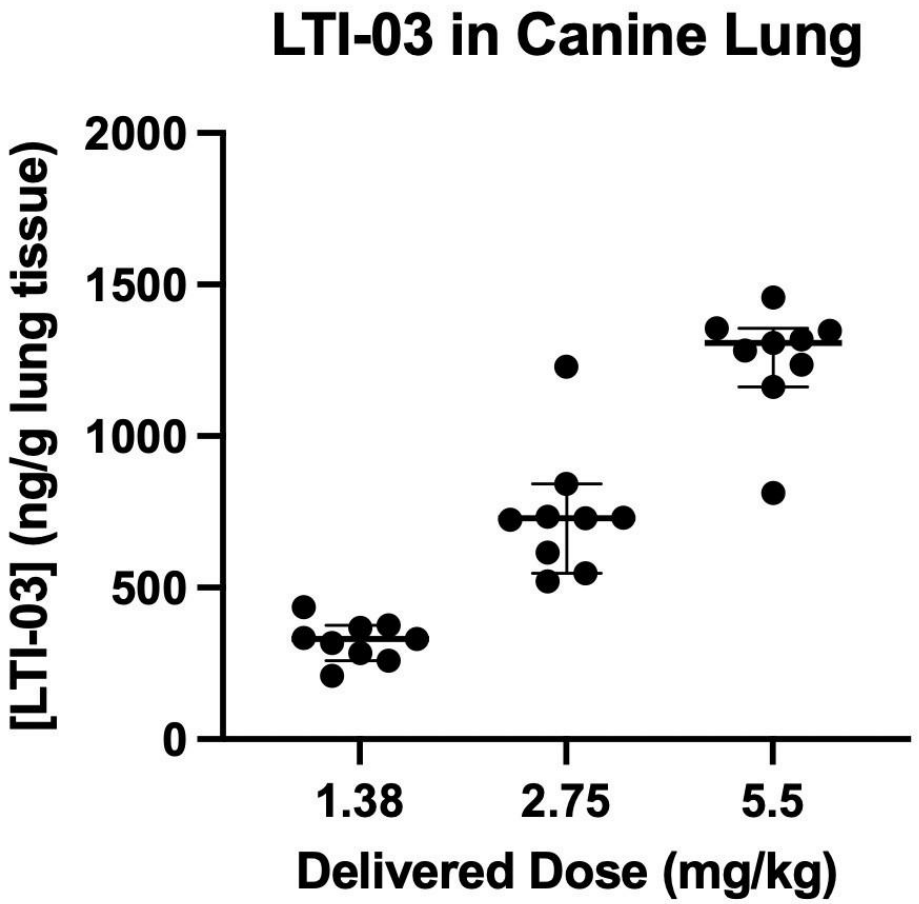


SOURCE: Zhang Y, MacKenzie B, Koleng JJ, Maier E, Warnken ZN, Williams RO III. Development of an Excipient-Free Peptide Dry Powder Inhalation for the Treatment of Pulmonary Fibrosis. Mol Pharm. 2020;17(2):632-644. doi:10.1021/acs.molpharmaceut.9b01085.



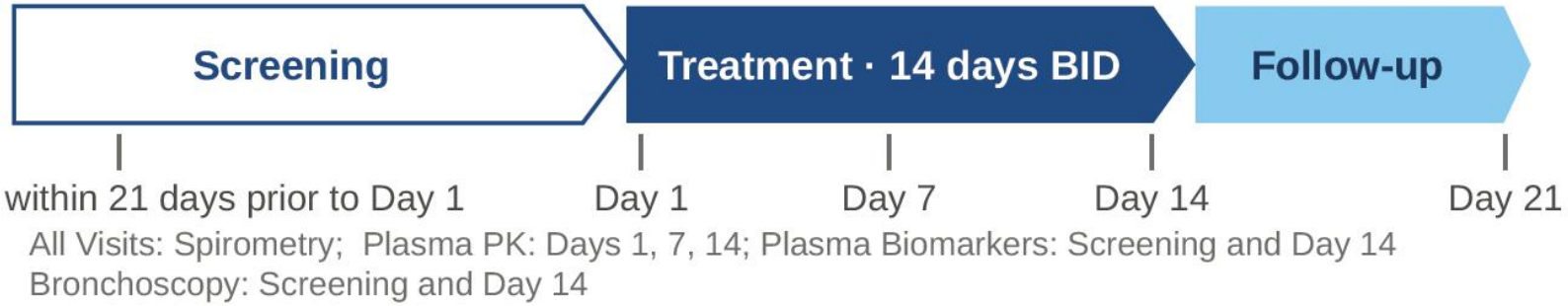
Pharmacokinetics of LTI-03

Intact LTI-03 was detected via LC-MS in the canine lung 24hrs post dose



LTI-03 was quantifiable in BALF but below quantification in plasma at every timepoint in the Ph1b study (NCT05954988)

STUDY DESIGN & METHODS



MINIMAL SYSTEMIC EXPOSURE

BALF: LTI-03 was detected in the lung

LTI-03 was quantifiable in Day-14 BALF in 5 active-treated participants: 3/9 (5 mg/day) and 2/9 (10 mg/day); 1.37–14.7 ng/mL.
All other collected BALF samples were BLQ.

PLASMA: LTI-03 was not quantifiable

Plasma LTI-03 was below the limit of quantification (BLQ) at all sampled post-dose timepoints (Days 1, 7, 14) indicating minimal systemic exposure.

- LTI-03 LLOQ: 1ng/mL
- LTI-03 detection rate was not dose-ordered given BALF collection variability

Source: Molyneaux, P. L. et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. *Nat. Commun.* **17**, 7620 (2026). https://doi.org/10.1038/s41467-026-75291-3

Translating efficacious dosing of LTI-03 (dry powder / clinical formulation)

A 1mg inhaled dose of LTI-03 would give an equivalent lung epithelial lining fluid (ELF) concentration of ~10uM (efficacious dose of LTI-03 in vitro is ~10uM)

Parameter	Value	Units
***In vitro* minimum efficacy**	10	µM
Molecular weight	815.91	Da
µg/mL from µM solution	8.16	µg/mL
Frohlich, 2016[15] - ELF volume	25	mL
Dose in device (nominal)	1.0	mg
Device Efficiency: Lonza	59%	%
Deposition Factor: MPPD3	42.8%	%
mg in lung ELF	0.25	mg
ELF Concentration	10.1	µg/mL
%Solubility	92.4%	%
ELF Conc + %Solubility	9.3	µg/mL
Margin above efficacy	1.1	fold

Table 1: LTI-03 dose translation from in vitro (cell culture based) to in vivo (human) doses.
ELF: epithelial lining fluid; **MPPD3**: median aerodynamic diameter

Nominal Dose (mg)	ELF Conc. (ug/mL)	%Solubility	In Vitro Margin
1	10.1	92.4%	1.1
2.5	25.3	91.9%	2.8
5	50.6	90.9%	5.6
10	101.1	89.1%	11.0
20	172	85.3%	21.1
40	404.4	77.8%	38.6

[a]in vitro margin as compared to 8.16 µg/mL

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BLM mouse efficacy study doses approximated a 9mg human dose

Value	Units	Parameter
0.13	mg/L	Measured aerosol concentration
11	min	Duration of exposure
0.035	kg	Mouse body weight (BW)
0.035	LPM	Calculated: Alexander, 2008[A]
1.43	mg/kg	**Delivered Dose[B]**
2.6%	%	Deposition Fraction (MPPD3)
0.037	mg/kg	Pulmonary Deposited Dose (PDD)
60	kg	Human BWT
2.2	mg	Mouse PDD x human BWT
59%	%	Emitted Dose: Lonza
42.8%	%	Deposition Factor (MPPD3)
9	**mg**	**Human Equivalent Dose (HED)[C]**

[A]**RMV**(L/min) = 0.608 × BW(Kg)$^{0.852}$

[B]**DD**= C x RMV x D x DF / BW RMV = respiratory minute volume (mouse)

DD = delivered dose (mg/kg)
C = concentration (mg/L)
RMV = respiratory minute (L/min)
D = duration of exposure (min)
DF = Deposition Factor (%)
BW=Body Weight (kg)

[C]**HED** = HuBW (kg) x muPDD / (%ED x DF)

muPDD = Pulmonary Deposited Dose
%ED = Device % emitted dose

Symposium Summary: "Breathe In, Breathe Out, Its Easy: What You Need to Know About Developing Inhaled Drugs"

International Journal of Toxicology
1-17

DOI: 10.1177/1091581815624080
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SAGE

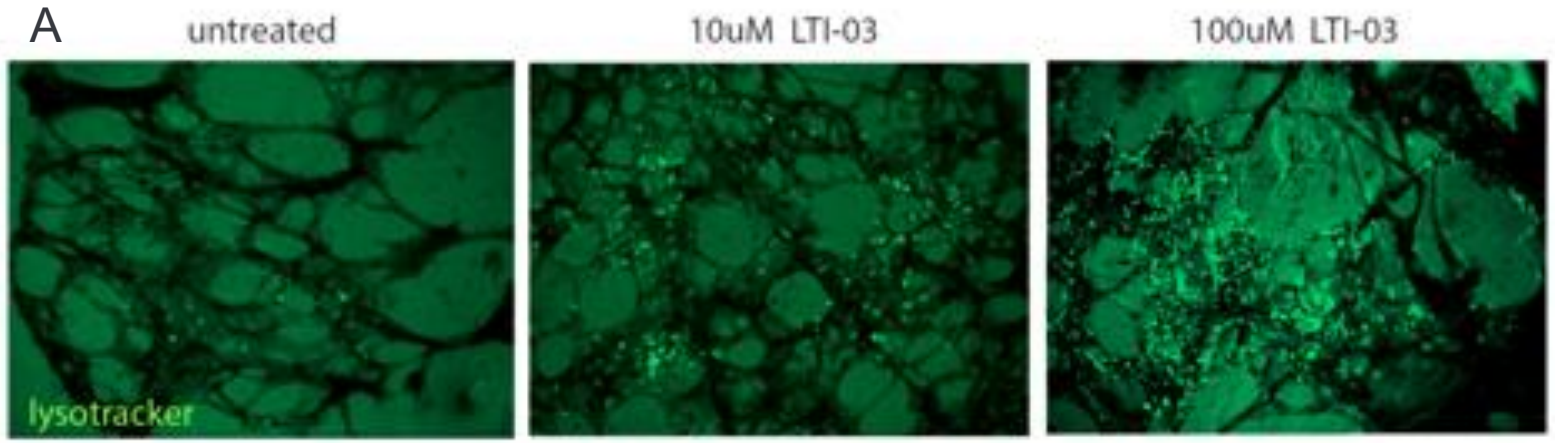
Jeffrey S. Tepper[1], Philip J. Kuehl[2], Stuart Cracknell[3], Kristen J. Nikula[4], Luqi Pei[5], and James D. Blanchard[6]

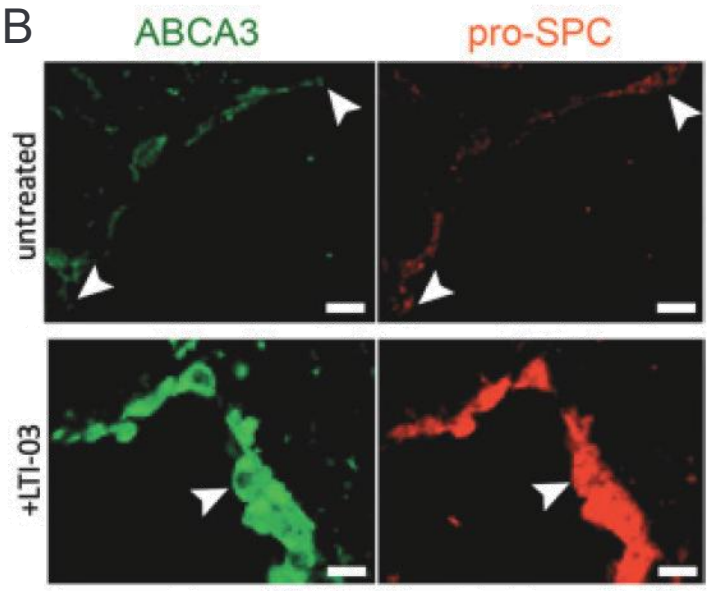
Evidence of alveolar restoration by LTI-03

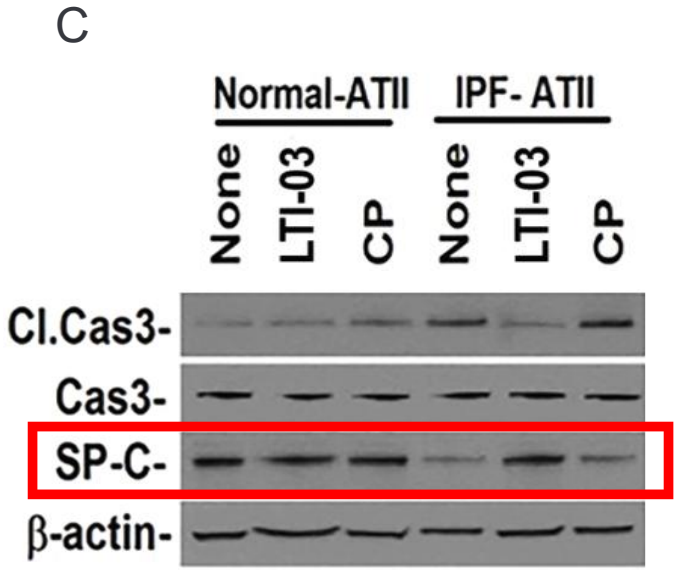
Increased LysoTracker signal, consistent with preserved or increased AEC2 lamellar body content; corroborated by increases in pro-SPC and ABCA3

(PCLS Studies. Effects 48 Hours After Administration)

- Lysotracker dye (Panel A, bright green dots) localizes to AEC2 cells, the progenitor cells of the lung, which are responsible for making new lung tissue. LTI-03 resulted in an increase in staining, meaning an increase in these critical progenitor cells
- Increases in lysotracker staining (Panel B) also correlated with increases in surfactant protein C (pro-SPC) and ABCA3 (the pro-SPC transporter)
- Western blots (Panel C) confirm that in the IPF lung SPC levels are diminished, but that LTI-03 causes levels to increase

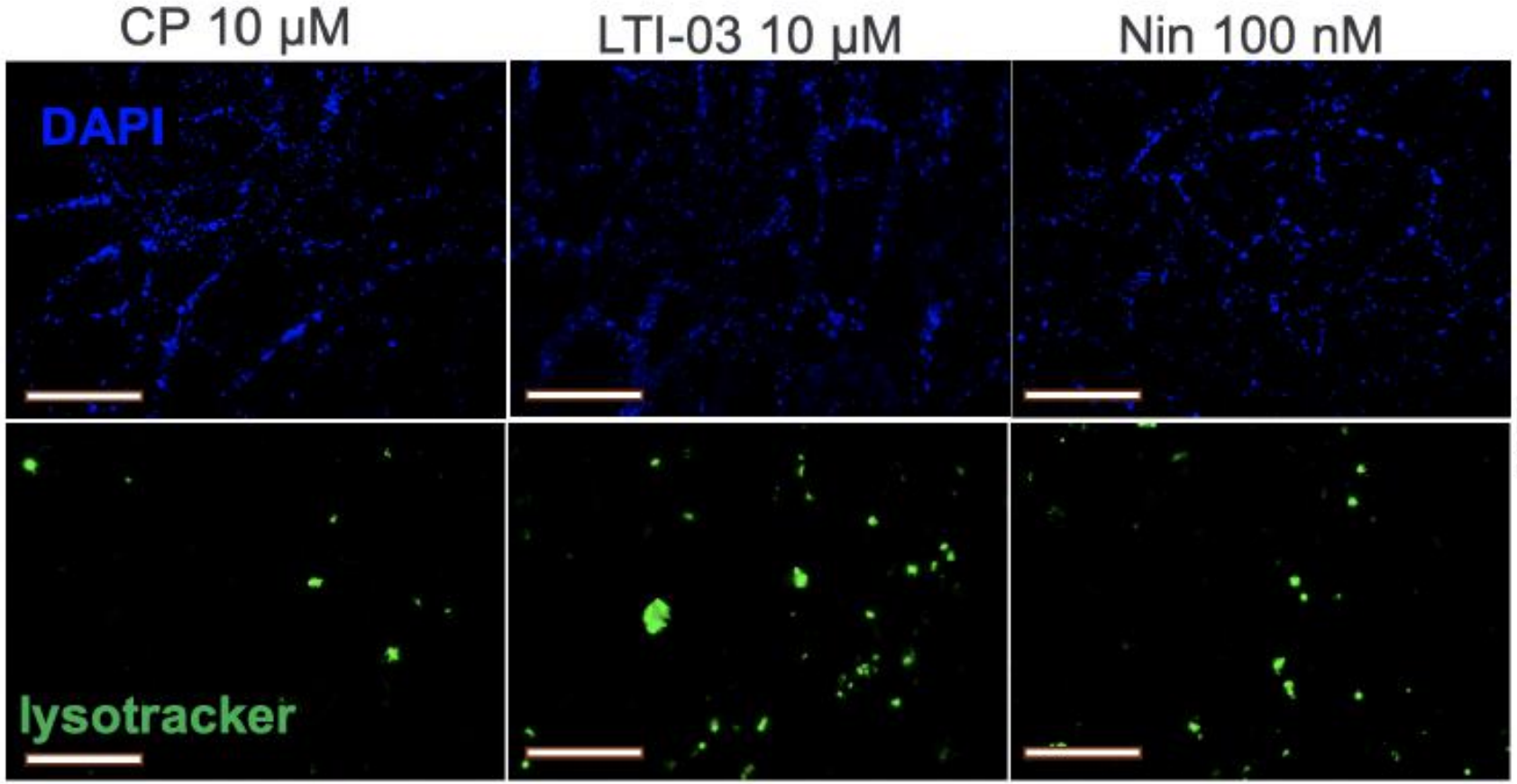


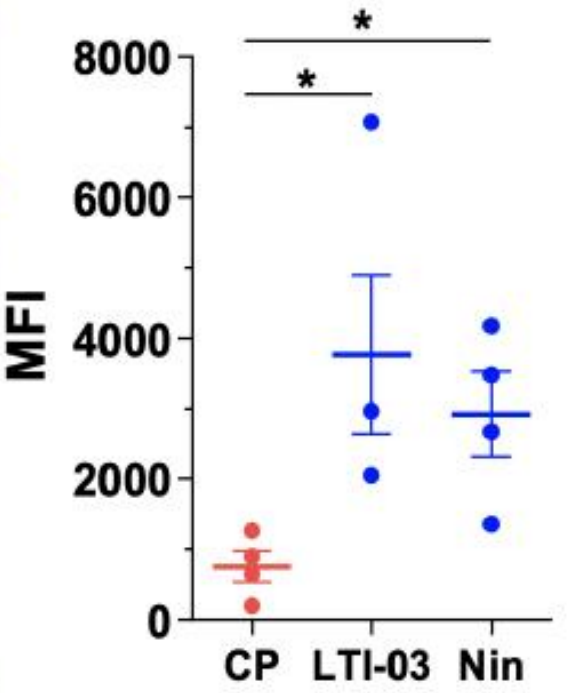




SOURCE: 2019, ERS International Congress. MacKenzie BA et al. Late Breaking Abstract - Caveolin-1 derived peptide LTI-03 promotes epithelial cell survival and attenuates pulmonary fibrosis. Eur Respir J. 2019;54(Suppl 63):PA1299. doi:10.1183/13993003.congress-2019.PA1299.

LTI-03 increased lysotracker staining in IPF precision cut lung slices (PCLS) indicating a positive effect on AEC2 cells

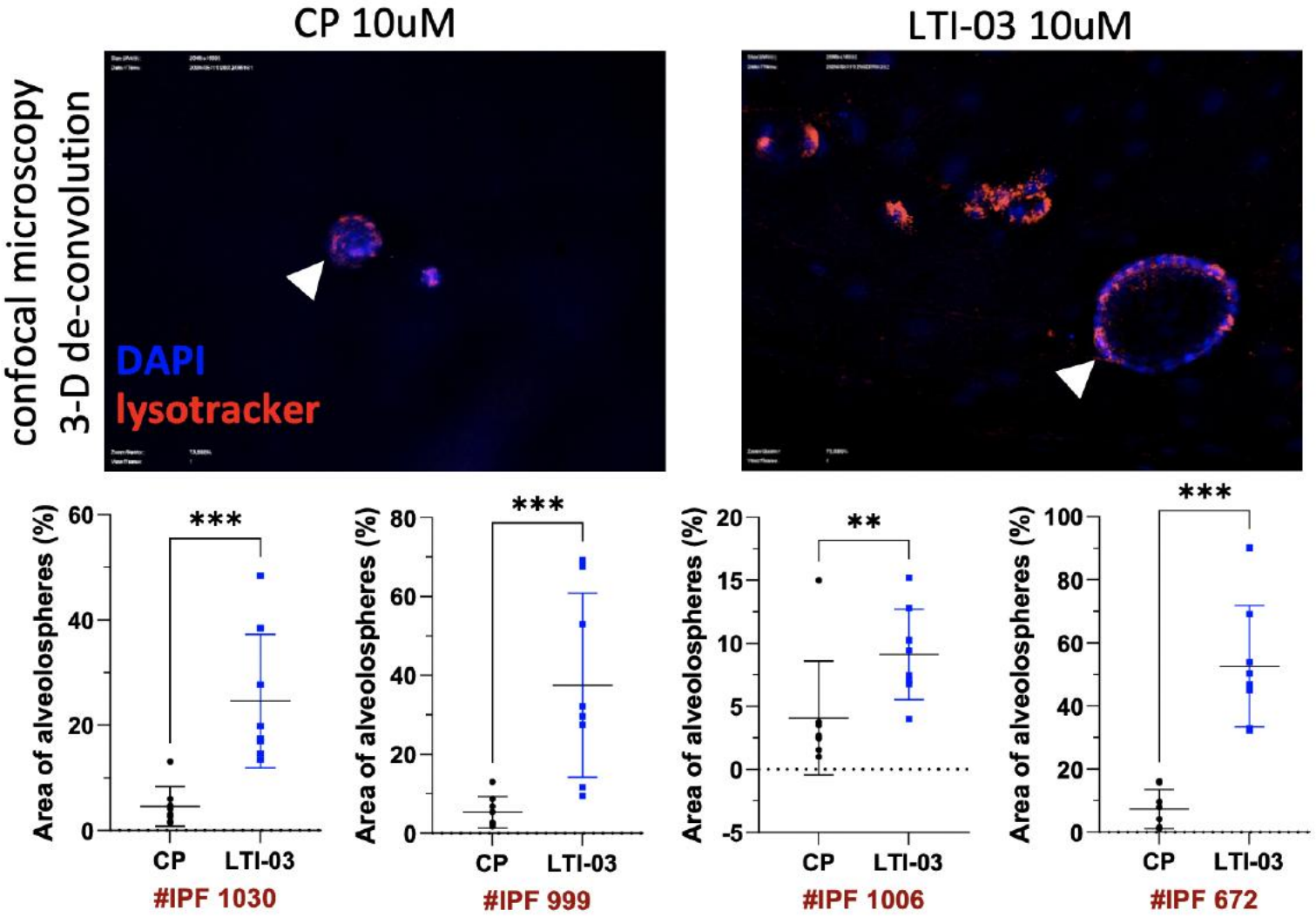




MFI: mean fluorescence intensity

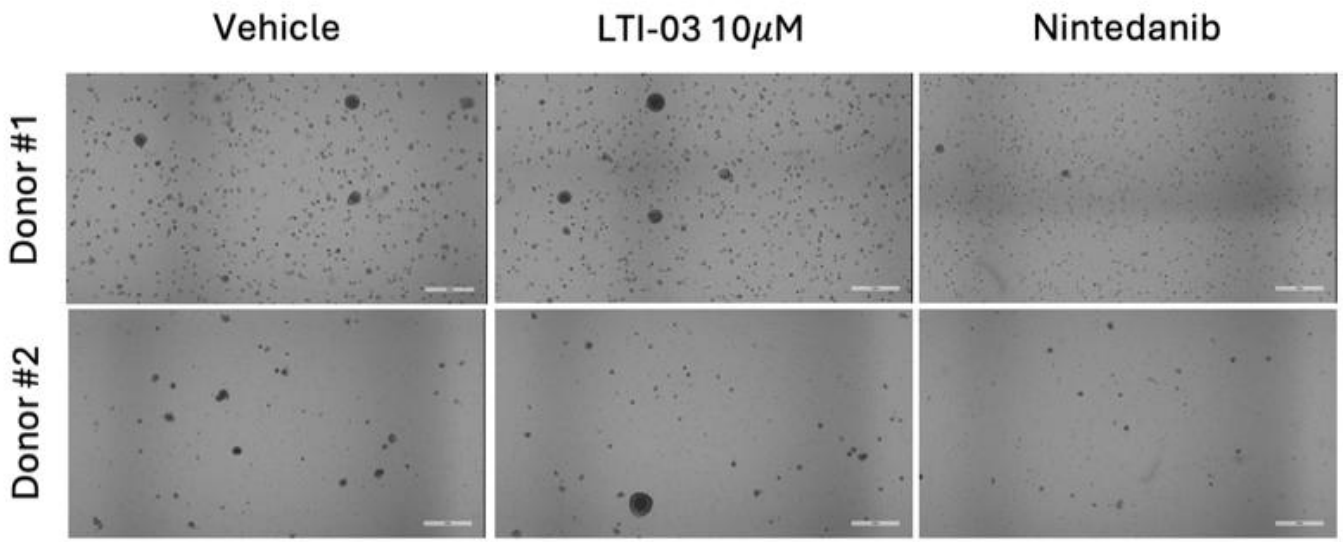
SOURCE: 2025, ATS International Conference. Jannini-Sa YAP, Coelho AL, MacKenzie B, Hogaboam CM. Evaluating Alveolar Regenerative Properties of Caveolin Scaffolding Peptides (CSD) in Three Dimensional (3D) Alveolospheres From IPF and Normal Donor Lung Samples. Am J Respir Crit Care Med. 2025;211(Suppl 1):A4691. doi:10.1164/ajrccm.2025.211.Abstracts.A4691.

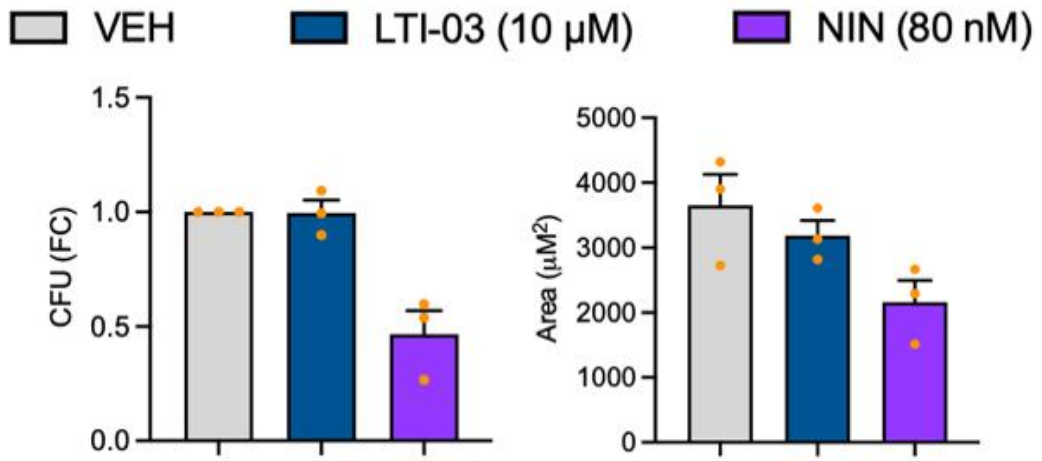
LTI-03 treatment increased alveolar organoid area in 4 distinct IPF patients



SOURCE: 2025, ATS International Conference. Jannini-Sa YAP, Coelho AL, MacKenzie B, Hogaboam CM. Evaluating Alveolar Regenerative Properties of Caveolin Scaffolding Peptides (CSD) in Three Dimensional (3D) Alveolospheres From IPF and Normal Donor Lung Samples. Am J Respir Crit Care Med. 2025;211(Suppl 1):A4691. doi:10.1164/ajrccm.2025.211.Abstracts.A4691.

LTI-03 sustained donor lung organoid growth (n=2 donors)

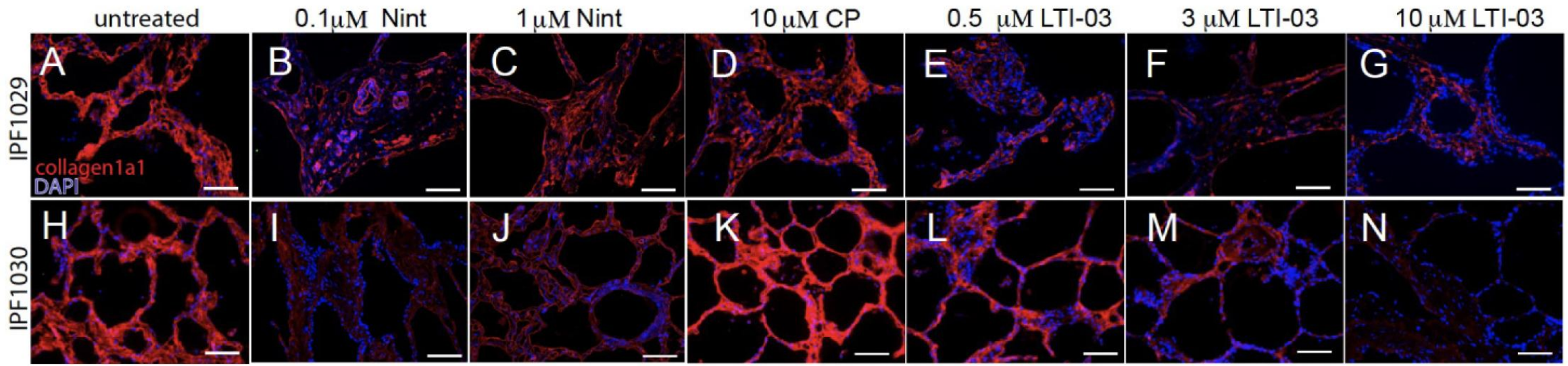


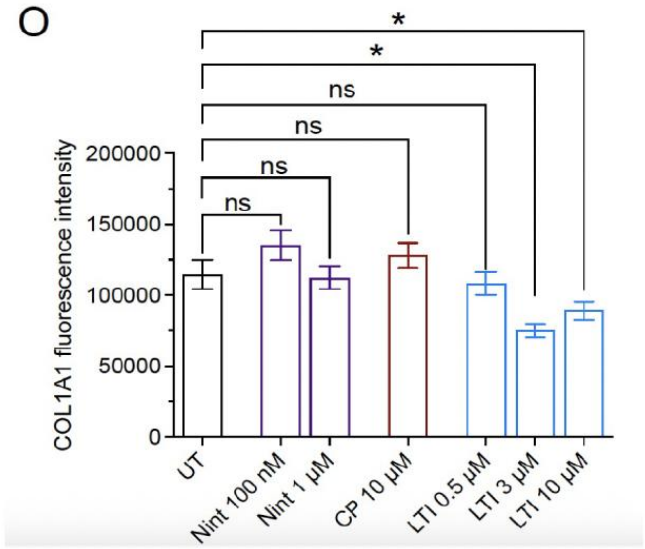


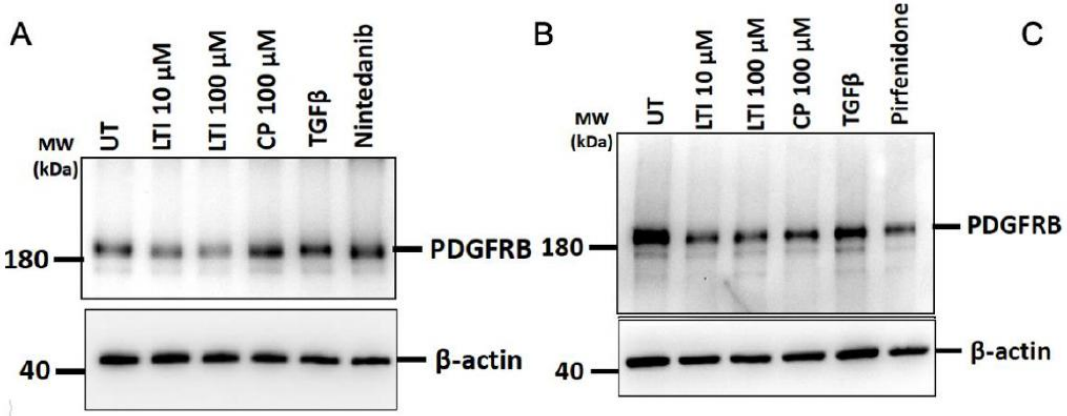
SOURCE: Adapted from 2025, ATS International Conference. Jannini-Sa YAP, Coelho AL, MacKenzie B, Hogaboam CM. Evaluating Alveolar Regenerative Properties of Caveolin Scaffolding Peptides (CSD) in Three Dimensional (3D) Alveolospheres From IPF and Normal Donor Lung Samples. Am J Respir Crit Care Med. 2025;211(Suppl 1):A4691. doi:10.1164/ajrccm.2025.211.Abstracts.A4691.

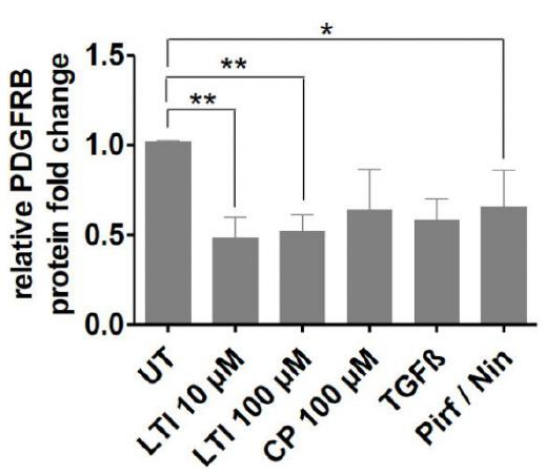
Evidence of anti-fibrotic effects of LTI-03 in preclinical fibrosis models

LTI-03 decreased COL1A1 and PDGFRB expression in end-stage IPF PCLS







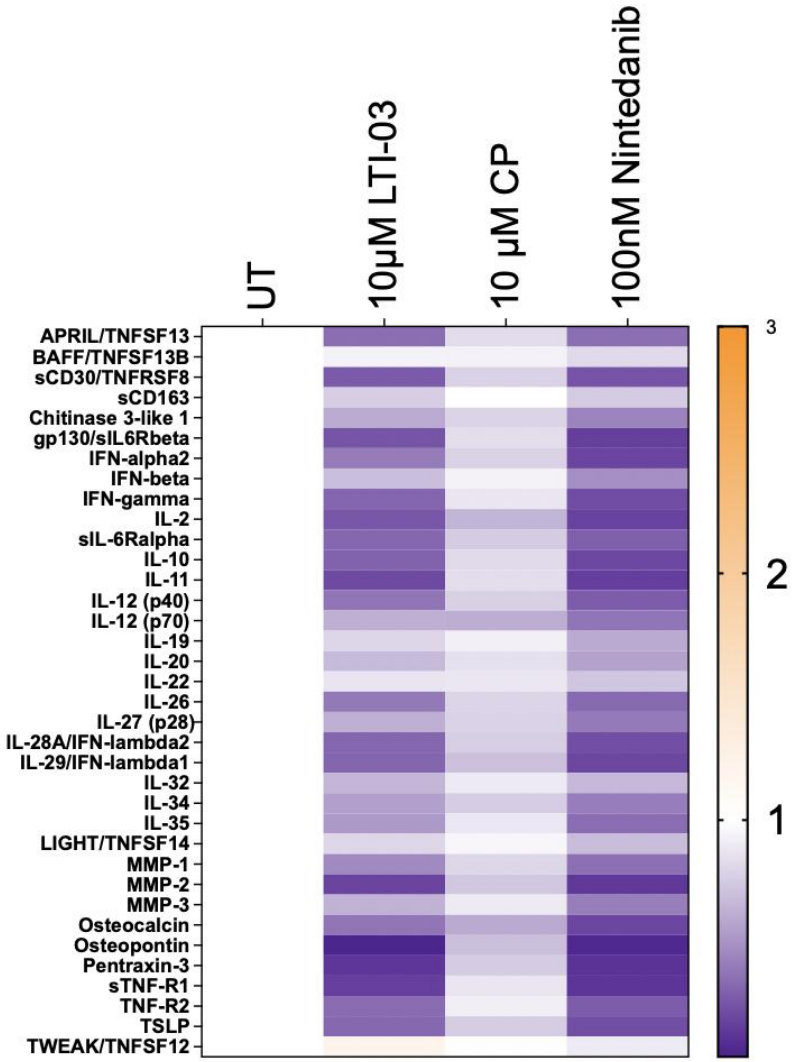


SOURCE: MacKenzie BA, Mahavadi P, Jannini-Sa YAP, et al. LTI-03 peptide demonstrates anti-fibrotic activity in ex vivo lung slices from patients with IPF. iScience. 2025;28:113437. doi:10.1016/j.isci.2025.113437.

Antifibrotic Activity: Single dose LTI-03 inhibits multiple profibrotic proteins similar to Ofev®

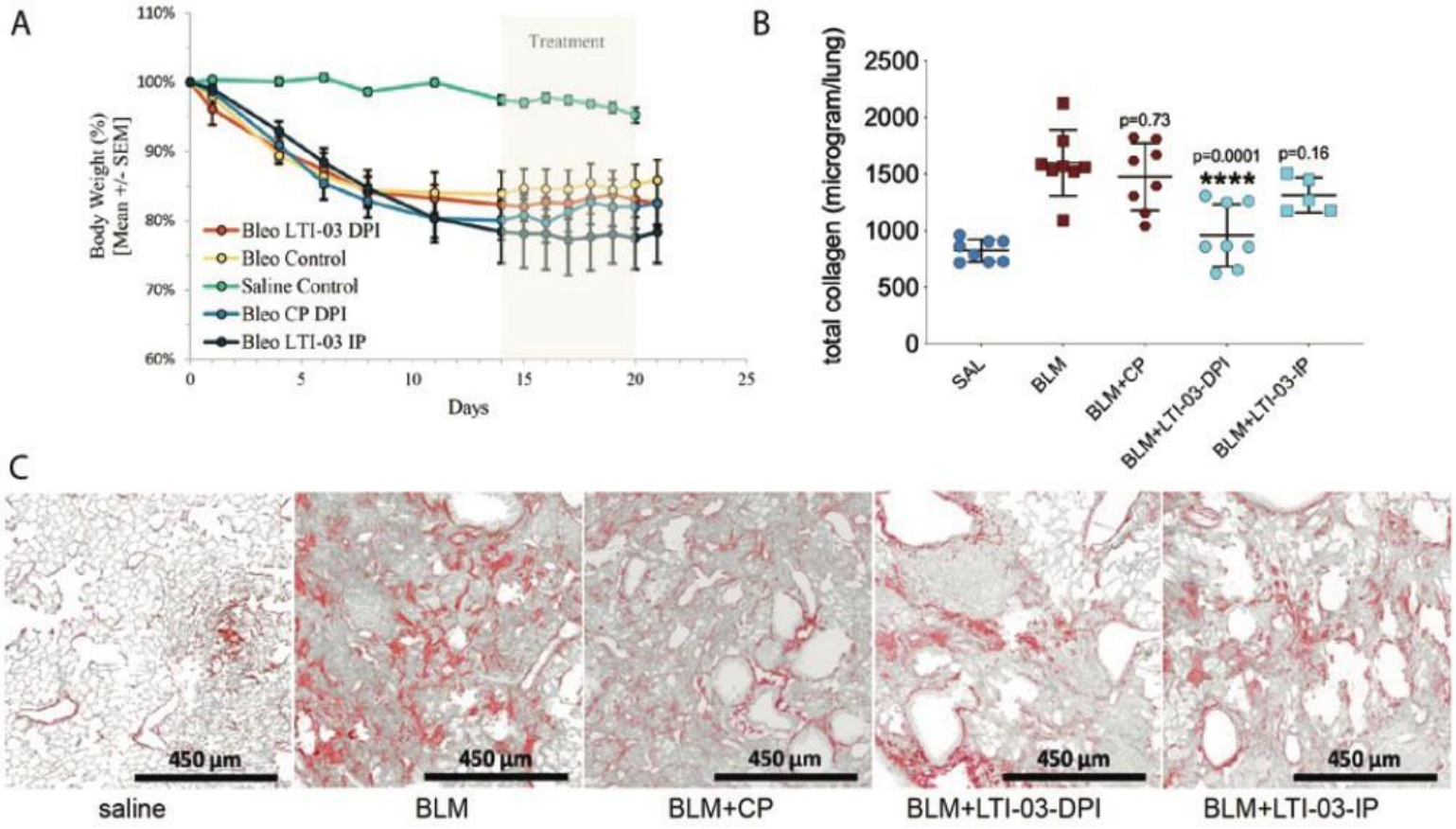
(Every 12hrs in Precision Cut Lung Slices (PCLS)—Single Patient Sample; CP: control peptide)

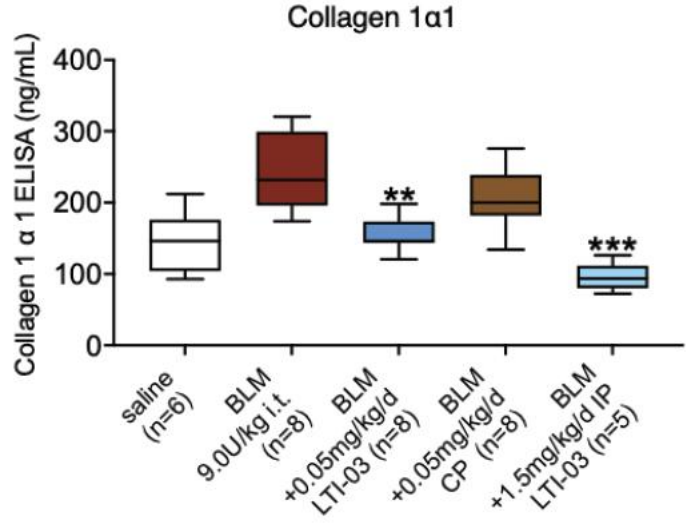
- As an **antifibrotic**, LTI-03 inhibits large panels of profibrotic proteins in a manner similar to the standard of care drug Ofev® (nintedanib)
  - Darker purple = more inhibition of the protein
- The PCLS tissue culture system uses actual biopsied tissue from an IPF lung (removed due to lung transplant), preserving all cell types in the IPF lung
- 10 µM LTI-03 is equivalent to an approximate dose of 1 mg in a dry powder inhaler. Phase 1b trial tested 5mg and 10mg, both of which were safe and well tolerated
- TSLP and IL-11 were attenuated by LTI-03 and Nintedanib

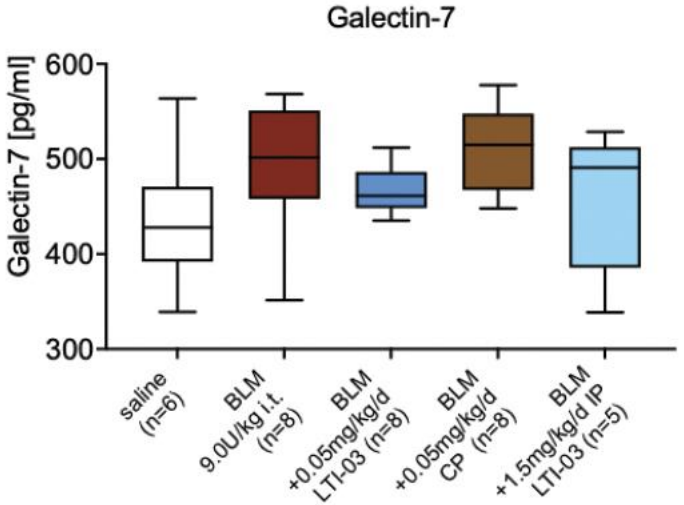


Day 4

Inhaled LTI-03 attenuated BLM induced fibrosis as well as COL1A1 and GAL7 in aged, male mice

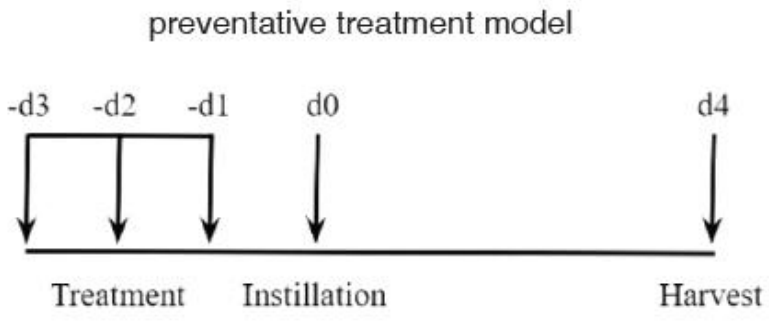


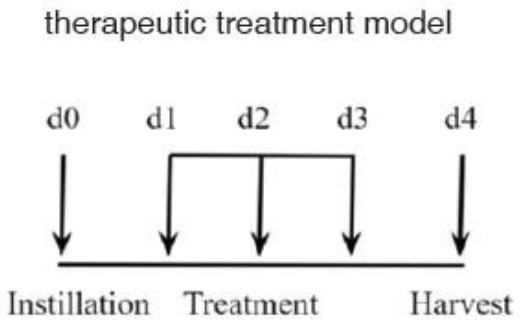




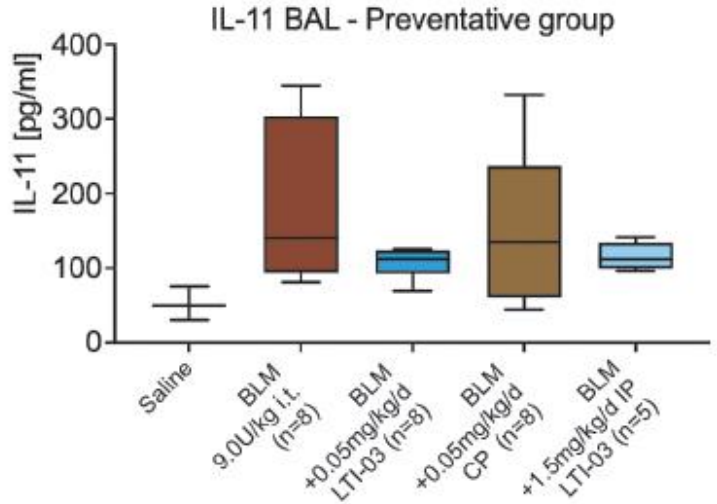
SOURCE: 2022, ATS International Conference. MacKenzie B, Maier E, Creyns B, Coelho AL, Windsor B, Hogaboam CM. Caveolin Scaffolding Domain LTI-03 Modulates Both Inflammatory and Fibrotic Responses in Aged Mice After Bleomycin Challenge. Am J Respir Crit Care Med. 2022;205(Suppl 1):A2307. doi:10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A2307.

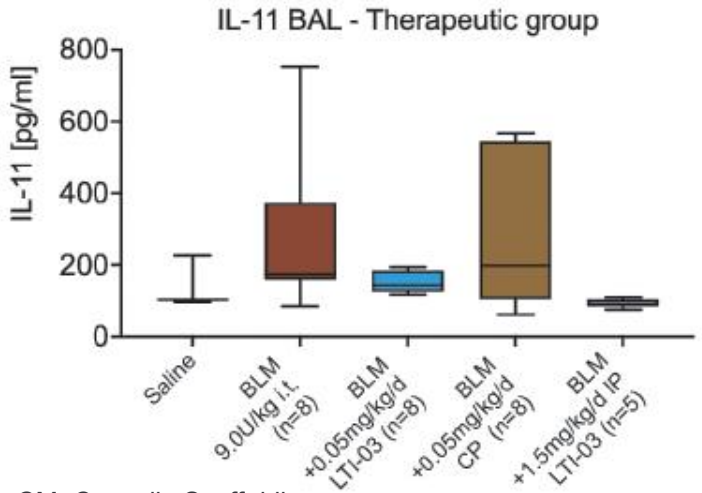
Inhaled LTI-03 attenuated IL-11 in BAL of aged, male mice in an acute lung bleo lung injury model when administered preventatively or prophylactically





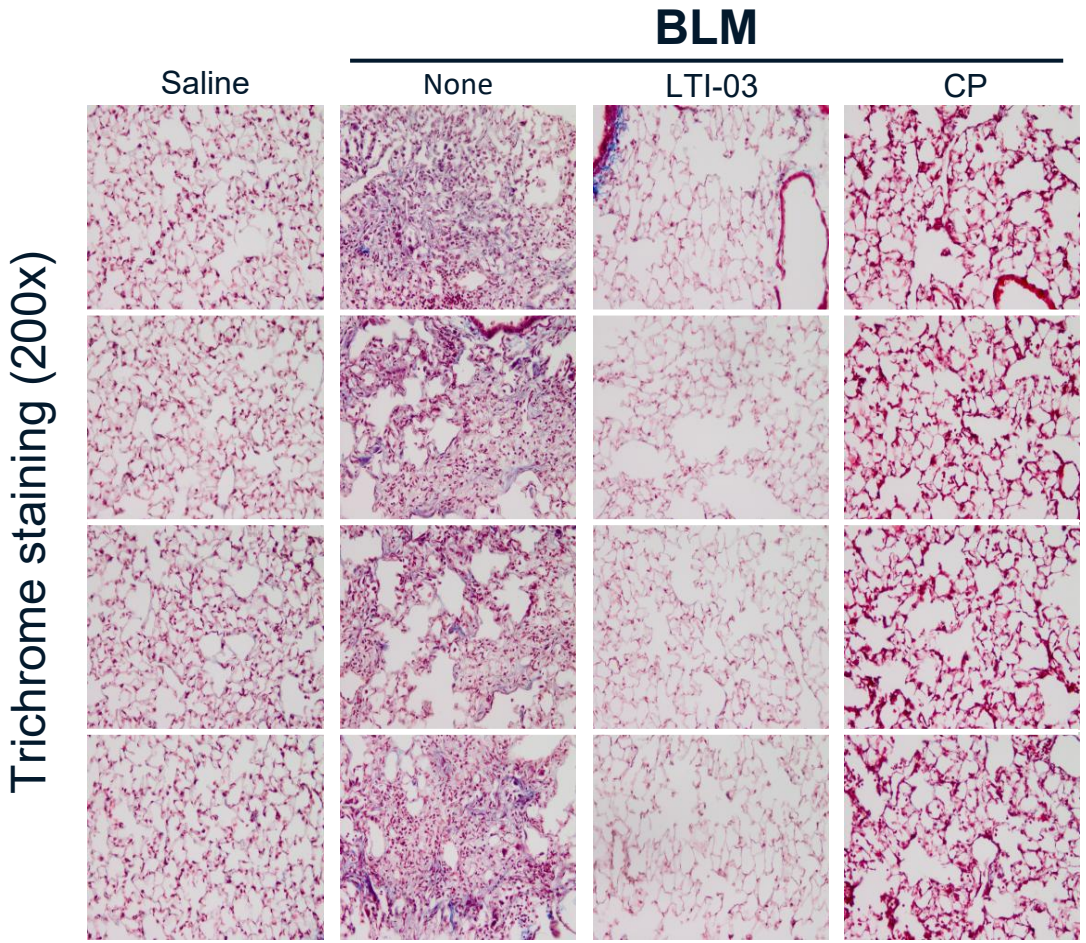
Group	Description	Bleomycin Dose [U/kg]	Treatment	Dose	Route	Therapeutic		Preventative	
A	Saline Control	None (Saline)	None	0	-	At	$n = 3$	Ap	$n = 3$
B	Bleo LTI-03 DPI	10	LTI-03	0.05 mg /mouse	DPI	Bt	$n = 7$	Bp	$n = 7$
C	Bleo CP DPI	10	CP	0.05 mg /mouse	DPI	Ct	$n = 6$	Cp	$n = 6$
D	Bleo Control	10	None	0	-	Dt	$n = 7$	Dp	$n = 7$
E	Bleo LTI-03 IP	10	LTI-03	1.5 mg/kg	IP	Et	$n = 5$	Ep	$n = 5$
Total Animals: 56									



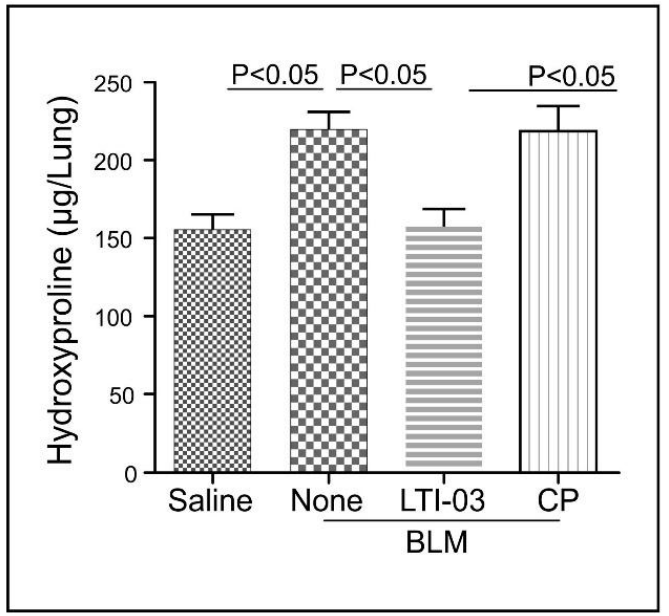


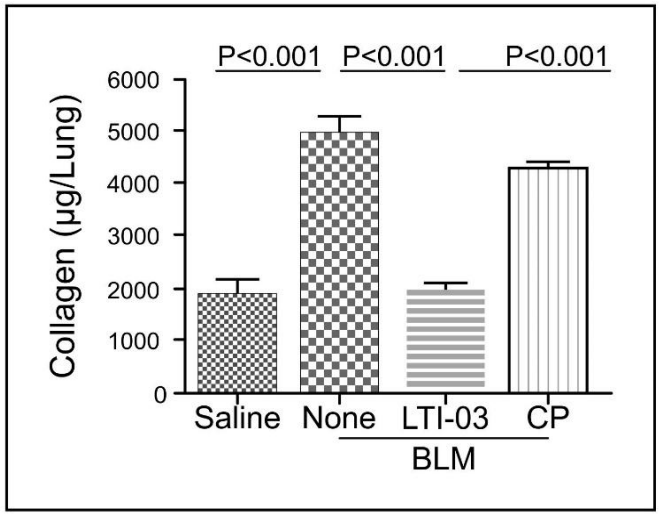
SOURCE: 2022, ATS International Conference. MacKenzie B, Maier E, Creyns B, Coelho AL, Windsor B, Hogaboam CM. Caveolin Scaffolding Domain LTI-03 Modulates Both Inflammatory and Fibrotic Responses in Aged Mice After Bleomycin Challenge. Am J Respir Crit Care Med. 2022;205(Suppl 1):A2307. doi:10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A2307.

Therapeutic dosing of inhaled LTI-03 (days 14 – 20) ameliorated fibrosis in the 21-day bleo mouse model of IPF



collagen measurements

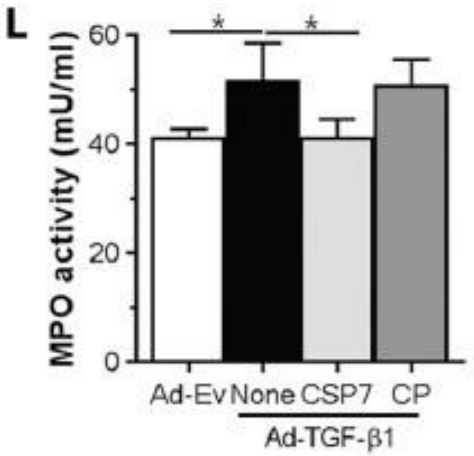


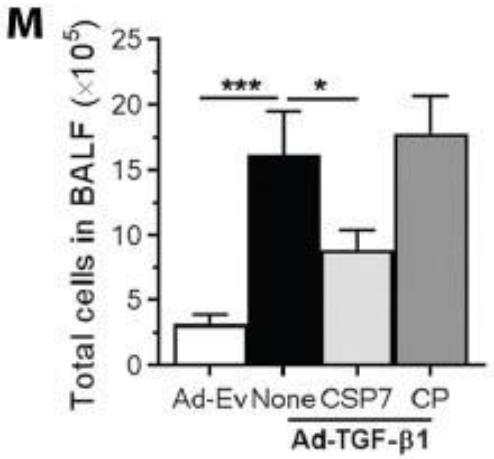


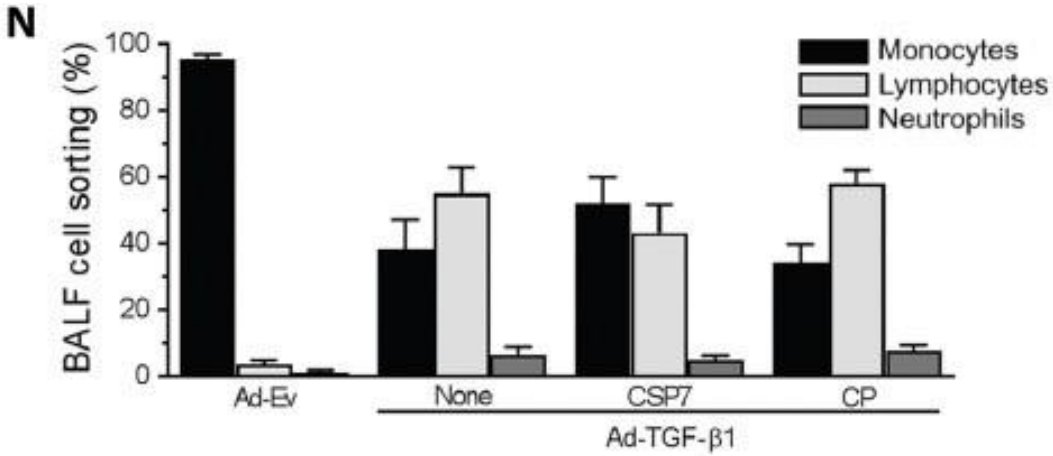
The bleomycin mouse model is the standard preclinical model for assessing anti-fibrotic activity; therapeutic dosing after fibrosis is established is the more stringent test

SOURCE: Marudamuthu AS, Bhandary YP, Fan L, et al. Caveolin-1-derived peptide limits development of pulmonary fibrosis. Sci Transl Med. 2019;11:eaat2848. doi:10.1126/scitranslmed.aat2848.

In both the Adv-TGFP and the BLM mouse models of fibrosis, LTI-03 reduced myeloperoxidase and immune cell recruitment to the lung





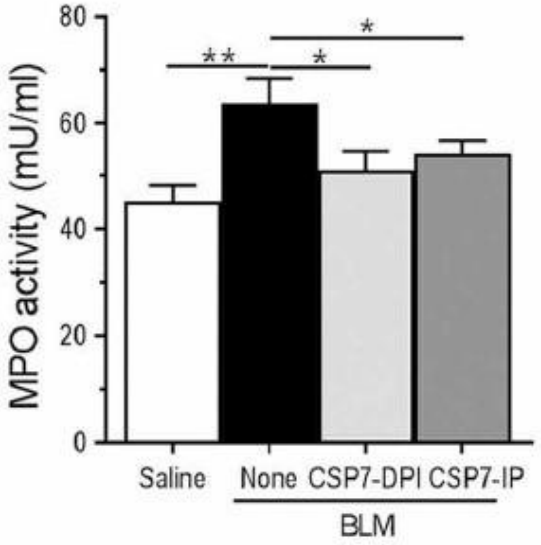


SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

PULMONARY FIBROSIS

Caveolin-1–derived peptide limits development of pulmonary fibrosis

Amarnath Satheesh Marudamuthu[1]*, Yashodhar Prabhakar Bhandary[1]*, Liang Fan[1]*, Vijay Radhakrishnan[1], BreAnne MacKenzie[2], Esther Maier[3], Shwetha Kumari Shetty[1], M. R. Nagaraja[1], Venkadesaperumal Gopu[1], Nivedita Tiwari[1], Yajie Zhang[3], Alan B. Watts[3], Robert O. Williams III[3], Gerald J Criner[4], Sudhir Bolla[4], Nathaniel Marchetti[4], Steven Idell[1], Sreerama Shetty[1†]



SOURCE: Marudamuthu AS, Bhandary YP, Fan L, et al. Caveolin-1-derived peptide limits development of pulmonary fibrosis. Sci Transl Med. 2019;11:eaat2848. doi:10.1126/scitranslmed.aat2848.

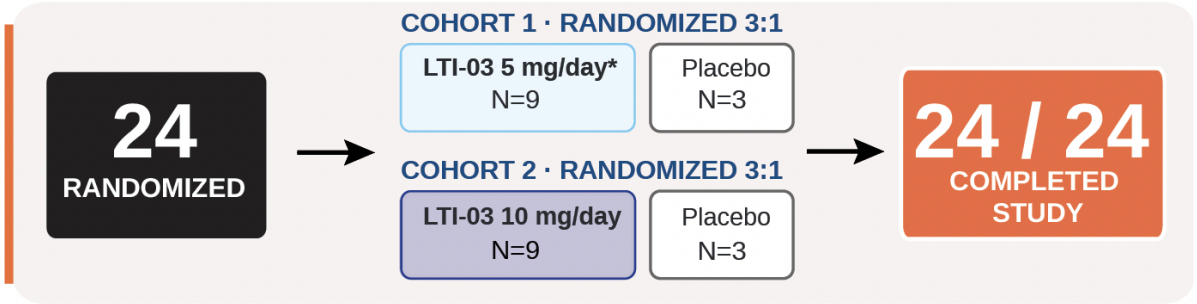
Evidence of LTI-03 biomarker activity in Ph1b clinical trial (NCT05954988)

Phase 1b (NCT05954988) Clinical Trial Design—Focus on Safety, Tolerability, and Biomarkers (Status: Complete)

STUDY DESIGN & METHODS

All Visits: Spirometry; Plasma PK: Days 1, 7, 14; Plasma Biomarkers: Screening and Day 14
Bronchoscopy: Screening and Day 14

PARTICIPANT DISPOSITION



*One participant (LTI-03 5 mg/day) had dosing stopped by Investigator decision on Day 14 after an FEV_1 decrease; however, the protocol's stopping criteria, which also required a decrease in FEV_1/FVC, were not met, and participant completed study. No participant discontinued due to TEAE.

GOOD SAFETY PROFILE

LTI-03 was well tolerated at both 5 and 10 mg/day.

No deaths, no severe (Grade ≥3) TEAEs, and no TEAEs leading to treatment discontinuation.
All 24 participants completed the study. Most TEAEs were mild (Grade 1).
The single serious TEAE, a Grade 2 post-bronchoscopy fever, was judged unrelated to study drug and resolved after overnight observation.

Participants, n (%)	LTI-03 5 mg/day (N=9)	LTI-03 10 mg/day (N=9)	Placebo (N=6)
Any TEAE	6 (66.7)	7 (77.8)	3 (50.0)
Related to study drug	2 (22.2)	5 (55.6)	1 (16.7)
Serious TEAE	0	1 (11.1)*	0
Grade ≥3 TEAE	0	0	0
Grade 2 TEAE	1 (11.1)	2 (22.2)	0
Cough	3 (33.3)	5 (55.6)	2 (33.3)
Rhinorrhea	1 (11.1)	1 (11.1)	0

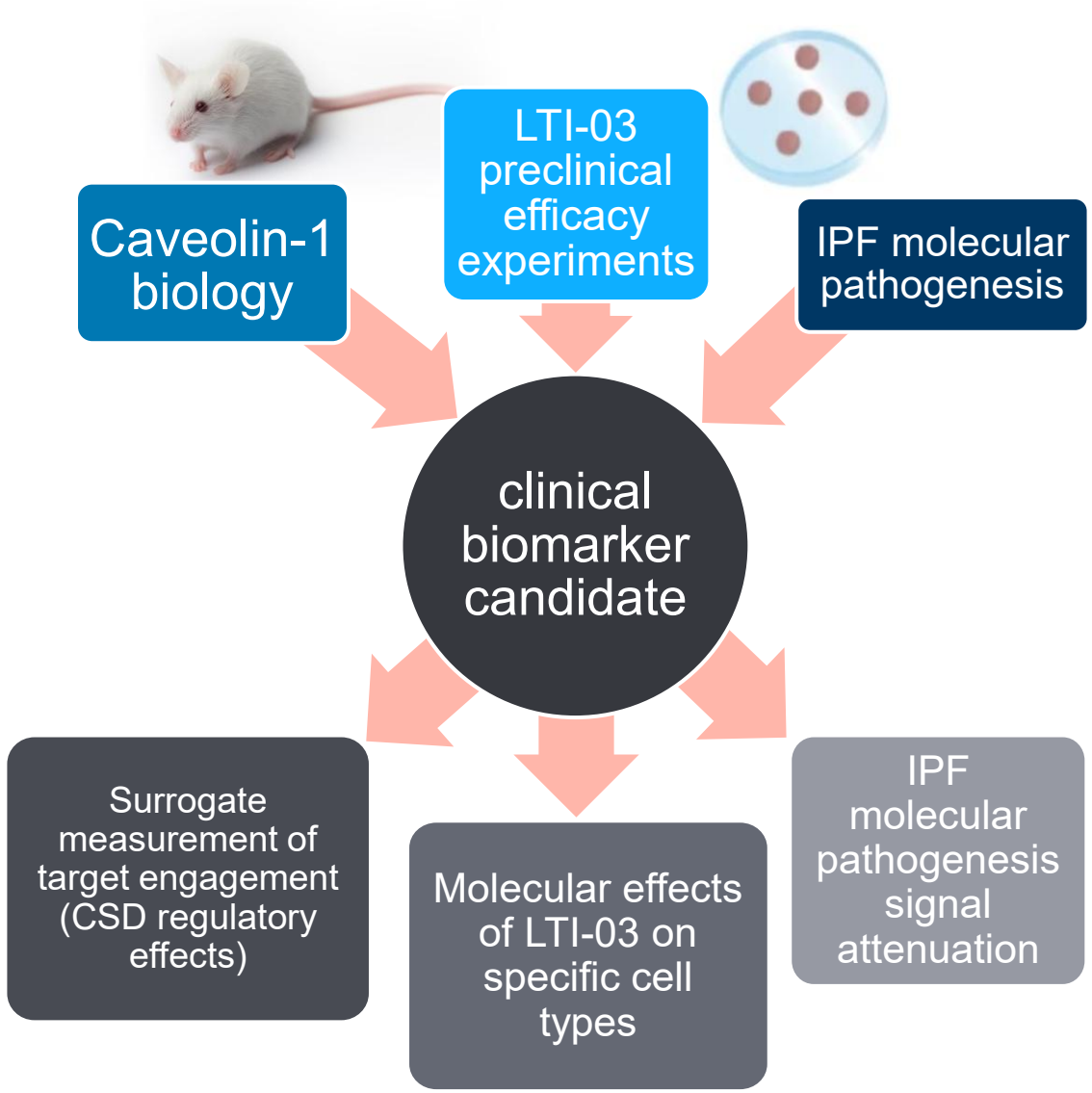
*Grade 2 post-bronchoscopy fever, unrelated to study drug (see above). Cough was the most common TEAE and the only drug-related TEAE in >1 participant; both Grade 2 coughs resolved the same day. TEAEs graded per CTCAE v5.

- No clinically significant changes in FEV_1 or FVC through Day 21; no evidence of airway obstruction by spirometry, and no chest tightness, non-exertional dyspnea, or wheezing.
- No treatment-related trends in labs, vitals, ECGs, or cough-related quality of life (LCQ/VAS)

SOURCE: 2026, ERS International Congress, Barcelona. Molyneaux PL et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. Late-breaking abstract accepted for ERS International Congress 2026. Public ERJ abstract number and DOI not yet indexed as of September 2, 2026.

REIN TX

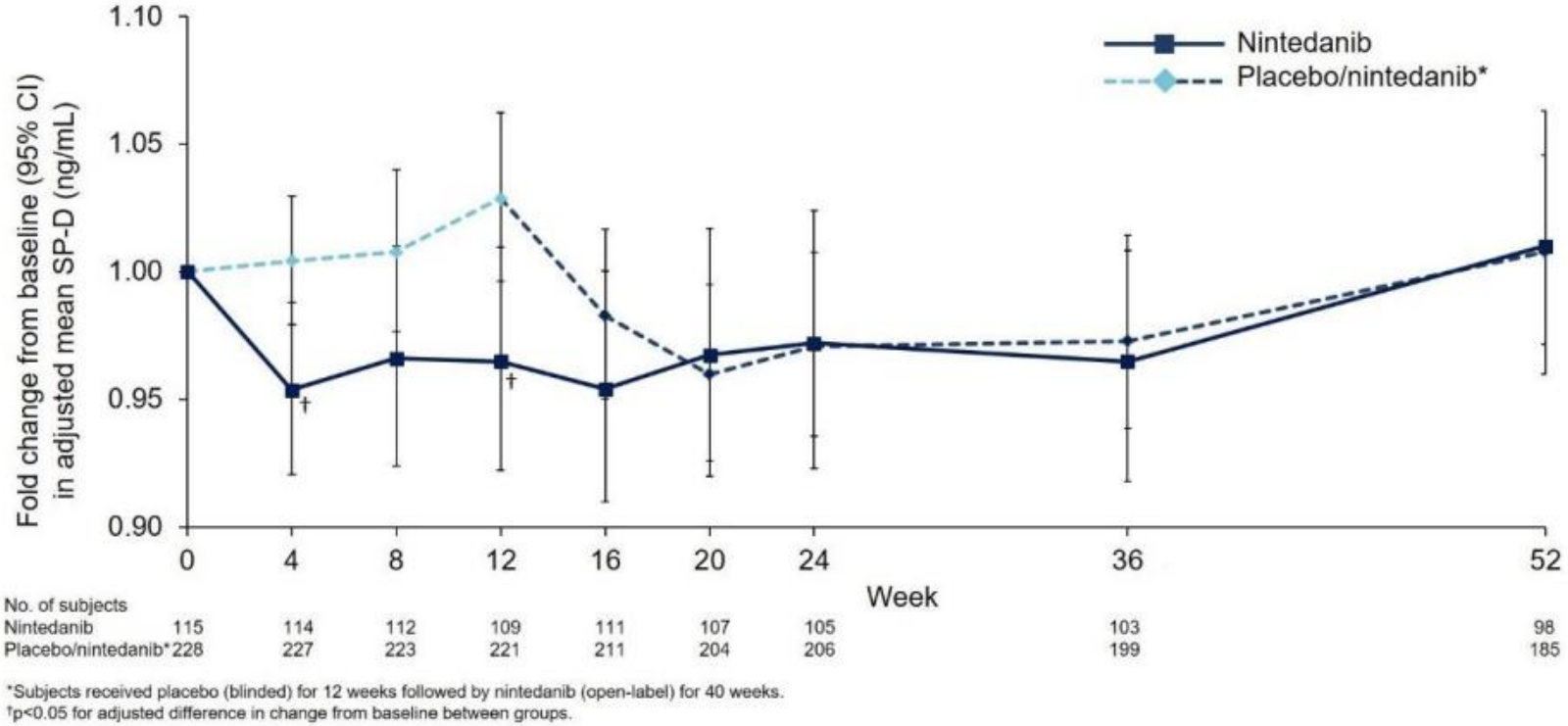
Ph1b exploratory biomarkers were pre-specified from nonclinical data and measured in plasma, peripheral blood mononuclear cells (PBMCs) and deep bronchial brushings (DBBs)



Matrix	Analytes	Method
Platelet-rich plasma	SP-D	MSD-ECL
PBMCs	pAKT / total AKT	MSD-ECL
DBBs	TSLP IL-11 COL1A1 CXCL7 GAL-7	ELISA

Surfactant Protein D (SPD) is an important biomarker for the approved IPF drug Ofev®*

- SPD is an indicator of epithelial cell health, an important cell type for proper lung function
- SPD has been significantly linked to decline in lung function
- SPD was reduced by 4% by Ofev over 12 weeks in the INMARK clinical trial
- **LTI-03 (10mg) <u>decreased plasma SPD by 4.6% over two weeks</u> in the Phase 1b trial;** (p=0.111; n=8 vs 5 pooled placebo; exploratory)



Nintedanib versus placebo. Fold changes from baseline in SP-D at week 12 corresponded to a 4% decrease and 3% increase in the nintedanib and placebo groups, respectively (ratio 0.94 [95% CI: 0.89, 0.99]; p=0.024).

*Jenkins RG, Cottin V, Nishioka Y, et al. Effects of nintedanib on circulating biomarkers of idiopathic pulmonary fibrosis. ERJ Open Res 2024; 2024;10(6):00558-2023.

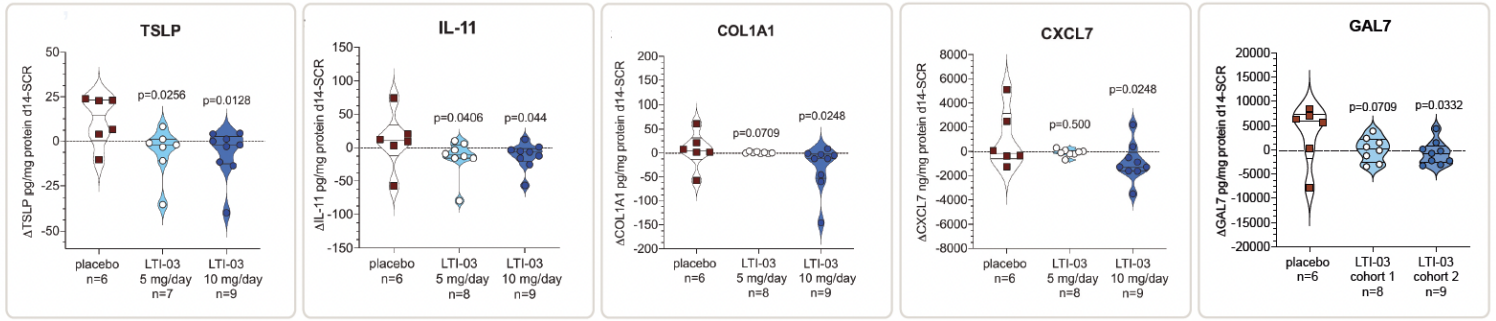
SOURCE: Molyneaux, P. L. et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. *Nat. Commun.* **17**, 7620 (2026). https://doi.org/10.1038/s41467-026-75291-3

REIN TX

LTI-03 Ph1b exploratory biomarkers assayed in deep bronchial brushings reached nominal significance (one-tailed Mann-Whitney vs pooled placebo; unadjusted for multiplicity); no significant change in p-AKT/AKT in PBMCs

- All exploratory biomarkers have:
  - ✓ Supporting literature suggesting their involvement in IPF pathogenesis
  - ✓ Are primarily found in important cell types in the IPF lung
  - ✓ Been shown in preclinical studies to be attenuated by LTI-03
- Ph1b data suggests:
  - ✓ LTI-03 biomarker attenuation is consistent with target engagement
  - ✓ LTI-03 is positively affecting pathogenic factors in the IPF lung

	COHORT 1: LTI-03 5 mg/day	COHORT 2: LTI-03 10 mg/day
TSLP	↓ p=0.026	↓ p=0.013
IL-11	↓ p=0.041	↓ p=0.044
COL1A1	ns (p=0.071)	↓ p=0.025
CXCL7	ns (p=0.500)	↓ p=0.025
GAL7	ns (p=0.071)	↓ p=0.033
Nominal one-tailed p<0.05:	2 / 5	5 / 5



DBBs were collected from basilar segments of the right lower lobe; analytes were quantified by ELISA and normalized to total protein.
Total samples COHORT 1: 5 mg/day DBB n=8; Total sample COHORT 2 10 mg/day DBB n=9; Total samples placebo n=6.
The reduced COHORT 1 n was due to a missed Day-14 DBB collection, and an additional TSLP value was BLQ.

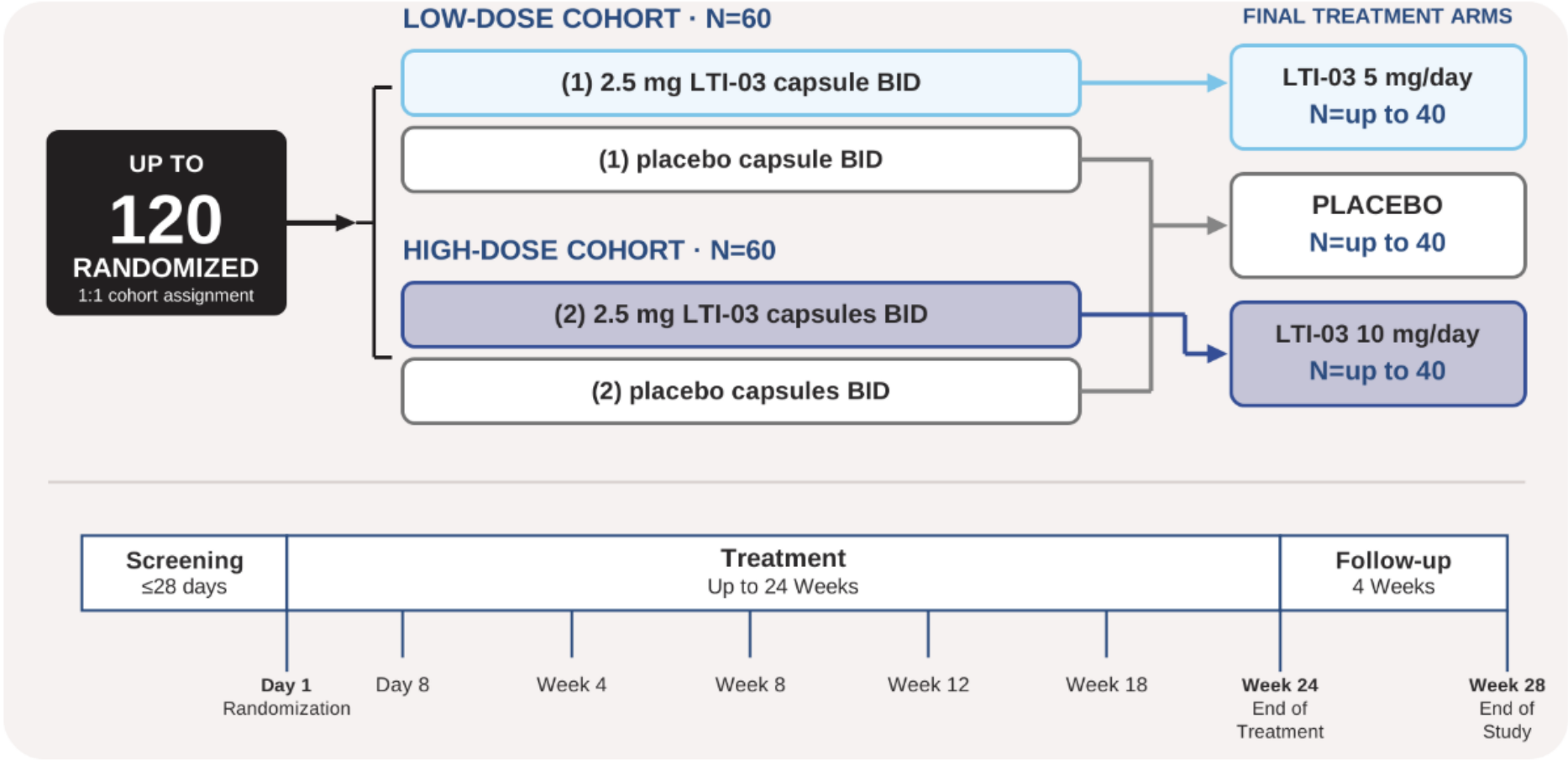
PBMC p-AKT/AKT (no significant change)

No significant change in PBMC p-AKT/total AKT was observed at either LTI-03 dose, indicating no measurable treatment-related effect on this peripheral signaling endpoint.

SOURCE: 2026, ERS International Congress, Barcelona. Molyneaux PL et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. Late-breaking abstract accepted for ERS International Congress 2026. Public ERJ abstract number and DOI not yet indexed as of September 2, 2026.

LTI-03 RENEW Phase 2 Trial (NCT06968845) NOW ENROLLING

RENEW STUDY DESIGN



RENEW
IPF CLINICAL STUDY

Phase 2 IPF Trial

clinicaltrials.gov:NCT06968845

Nasdaq: RNTX

Appendix

Peer reviewed supporting publications

1. Molyneaux PL et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. Nat Commun. 2026;17:7620. doi:10.1038/s41467-026-75291-3.

2. Fan L, Shetty RS, Dao HM, et al. p53-miR-34a feedback in lung fibroblasts regulates antifibrotic effects of CSP7, nintedanib, and pirfenidone. Am J Physiol Lung Cell Mol Physiol. 2025;329:L480-L498. doi:10.1152/ajplung.00295.2024.

3. MacKenzie BA, Mahavadi P, Jannini-Sa YAP, et al. LTI-03 peptide demonstrates anti-fibrotic activity in ex vivo lung slices from patients with IPF. iScience. 2025;28:113437. doi:10.1016/j.isci.2025.113437.

4. Reese CF, Chinnakkannu P, Tourkina E, Hoffman S, Kuppuswamy D. Multiple subregions within the caveolin-1 scaffolding domain inhibit fibrosis, microvascular leakage, and monocyte migration. PLoS One. 2022;17:e0264413. doi:10.1371/journal.pone.0264413.

5. Kuppuswamy D, Chinnakkannu P, Reese C, Hoffman S. The Caveolin-1 Scaffolding Domain Peptide Reverses Aging-Associated Deleterious Changes in Multiple Organs. J Pharmacol Exp Ther. 2021;378:1-9. doi:10.1124/jpet.120.000424.

6. Zhang Y, MacKenzie B, Koleng JJ, Maier E, Warnken ZN, Williams RO III. Development of an Excipient-Free Peptide Dry Powder Inhalation for the Treatment of Pulmonary Fibrosis. Mol Pharm. 2020;17(2):632-644. doi:10.1021/acs.molpharmaceut.9b01085.

7. Marudamuthu AS, Bhandary YP, Fan L, et al. Caveolin-1-derived peptide limits development of pulmonary fibrosis. Sci Transl Med. 2019;11:eaat2848. doi:10.1126/scitranslmed.aat2848.

8. Chinnakkannu P, Reese C, Gaspar JA, et al. Suppression of angiotensin II-induced pathological changes in heart and kidney by the caveolin-1 scaffolding domain peptide. PLoS One. 2018;13(12):e0207844. doi:10.1371/journal.pone.0207844.

9. Surasarang SH, Florova G, Komissarov AA, Shetty S, Idell S, Williams RO III. Formulation for a novel inhaled peptide therapeutic for idiopathic pulmonary fibrosis. Drug Dev Ind Pharm. 2018;44(2):184-198. doi:10.1080/03639045.2017.1371736.

10. Tepper JS, Kuehl PJ, Cracknell S, Nikula KJ, Pei L, Blanchard JD. Symposium Summary: "Breathe In, Breathe Out, Its Easy: What You Need to Know About Developing Inhaled Drugs". Int J Toxicol. 2016;35(4):376-392. doi:10.1177/1091581815624080.

11. Tourkina E, Richard M, Gooz P, et al. Antifibrotic properties of caveolin-1 scaffolding domain in vitro and in vivo. Am J Physiol Lung Cell Mol Physiol. 2008;294(5):L843-L861. doi:10.1152/ajplung.00295.2007.

12. Wang XM, Zhang Y, Kim HP, et al. Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis. J Exp Med. 2006;203(13):2895-2906. doi:10.1084/jem.20061536.

13. Gvaramia D, Blaauboer ME, Hanemaaijer R, Everts V. Role of caveolin-1 in fibrotic diseases. Matrix Biol. 2013;32(6):307-315. doi:10.1016/j.matbio.2013.03.005

Peer reviewed supporting abstracts

1. 2026, ERS International Congress, Barcelona. Molyneaux PL et al. Inhaled LTI-03 for idiopathic pulmonary fibrosis: a randomized dose escalation study. Late-breaking abstract accepted for ERS International Congress 2026. Public ERJ abstract number and DOI not yet indexed as of September 2, 2026.

2. 2025, ATS International Conference. Jannini-Sa YAP, Coelho AL, MacKenzie B, Hogaboam CM. Evaluating Alveolar Regenerative Properties of Caveolin Scaffolding Peptides (CSD) in Three Dimensional (3D) Alveolospheres From IPF and Normal Donor Lung Samples. Am J Respir Crit Care Med. 2025;211(Suppl 1):A4691. doi:10.1164/ajrccm.2025.211.Abstracts.A4691.

3. 2025, ATS International Conference. Mahavadi P et al. Pre-clinical Proof-of-Concept of Anti-fibrotic Activity of Caveolin-1 Scaffolding Domain Peptide LTI-03 in Ex Vivo Precision Cut Lung Slices From Patients With Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med. 2025;211(Suppl 1):A4651. doi:10.1164/ajrccm.2025.211.Abstracts.A4651.

4. 2024, 22nd International Colloquium on Lung and Airway Fibrosis (ICLAF). Inhalation of LTI-03 Modulates Multiple Targets in a Phase 1B Placebo Controlled Clinical Trial for IPF. Abstract 0183.

5. 2024, 22nd International Colloquium on Lung and Airway Fibrosis (ICLAF). Anti-Fibrotic Activity of Caveolin-1 scaffolding domain Peptide LTI-03 in Ex Vivo Precision Cut Lung Slices from Patients with Idiopathic Pulmonary Fibrosis. Abstract 0186.

6. 2022, ATS International Conference. Creyns B, MacKenzie B, Coelho AL, Windsor JB, Hogaboam CM. Caveolin Scaffolding Domain (CSD) Peptide LTI-2355 Modulates Phagocytic and Synthetic Activity of Idiopathic Pulmonary Fibrosis (IPF) Myeloid Cells. Am J Respir Crit Care Med. 2022;205(Suppl 1):A5341. doi:10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A5341.

7. 2022, ATS International Conference. MacKenzie B, Maier E, Creyns B, Coelho AL, Windsor B, Hogaboam CM. Caveolin Scaffolding Domain LTI-03 Modulates Both Inflammatory and Fibrotic Responses in Aged Mice After Bleomycin Challenge. Am J Respir Crit Care Med. 2022;205(Suppl 1):A2307. doi:10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A2307.

8. 2020, ATS International Conference. Shetty S et al. Caveolin-1-Derived Peptide Limits Development of Pulmonary Fibrosis. Am J Respir Crit Care Med. 2020;201(Suppl 1):A7881. doi:10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A7881.

9. 2019, ERS International Congress. MacKenzie BA et al. Late Breaking Abstract - Caveolin-1 derived peptide LTI-03 promotes epithelial cell survival and attenuates pulmonary fibrosis. Eur Respir J. 2019;54(Suppl 63):PA1299. doi:10.1183/13993003.congress-2019.PA1299.

10. 2017, Pulmonary Fibrosis Foundation Summit. Surasarang SH et al. Resolution of a rodent model of pulmonary fibrosis with a novel peptide delivered by nebulization. Poster presented at the Pulmonary Fibrosis Foundation Summit, 2017.