REIN Therapeutics

Harnessing fibrosis, unleashing life

Corporate Presentation | January 2025

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 timing and expectation of a Phase 2 clinical trial of LTI-03; future expectations, plans and prospects for the Company; the sufficiency of the Company's cash resources; and the potential commercial opportunity of LTI-03 and LTI-01]. 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 risks and uncertainties related to changes in applicable laws or regulations, the possibility that the Company may be adversely affected by other economic, business, and/or competitive factors, including risks inherent in pharmaceutical research and development, such as: adverse results in the Company's drug discovery, preclinical and clinical development activities, the risk that the results of preclinical studies and early clinical trials may not be replicated in later clinical trials, including a Phase 2 clinical trial of LTI-03, or that partial results of a trial will be indicative of the full results of the trial, the Company's ability to enroll patients in its clinical trials, and the risk that any of its clinical trials may not commence, continue or be completed on time, or at all; decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies with respect to our development candidates; our ability to obtain, maintain and enforce intellectual property rights for our platform and development candidates; competition; uncertainties as to the sufficiency of the Company's cash resources to fund its planned activities for the periods anticipated and the Company's ability to manage unplanned cash requirements; and general economic and market conditions; as well as 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, 2023 and the Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, which are on file with the United States Securities and Exchange Commission (the "SEC"), 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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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**
- Pipeline of novel therapies with **two Phase 2-ready assets** with differentiated mechanisms of action: LTI-03 (IPF) & LTI-01 (LPE)
- **LTI-03** is a **potential blockbuster treatment** which has demonstrated antifibrotic and regenerative properties
  - **Unique dual mechanism** promoting alveolar epithelial cell survival & inhibiting profibrotic signaling
  - More favorable safety profile to date than Ofev® (current SOC; 2023 sales ~$3.6B)
  - KOL support for new, safer and effective therapies
- **LTI-01** has the **potential to be the first approved drug for LPE**, a challenging condition with complex pleural diseases
  - Demonstrated efficacy in Phase 1B & Phase 2a trials
  - Potential safety benefit and dosing advantage over off label fibrinolytics
  - Orphan Drug Designation in US & EU; Fast Track Designation in US
  - Partnership with Taiho Pharma for development & commercial rights in Japan

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Therapies for Underserved Fibrosis and Pulmonary Conditions

LTI-03 ***Idiopathic Pulmonary Fibrosis***	***Advancing into Phase 2***	• Phase 1 clinical met primary endpoint; High dose LTI-03 (5mg BID) was **well-tolerated** with **no observed safety issues** • Evaluated a robust set of **exploratory biomarkers** with **predictive value of lung health** • Results **validated preclinical & clinical findings** for key biomarkers with **dose-dependent effects**
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
LTI-05 ***Cystic Fibrosis***	***PC***	• ENaC inhibitor intended for the **15-20% of CF pts.** who **do not respond to CFTR modulators** • **100% inhibition** and **localized** activity (safety profile) in preclinical studies

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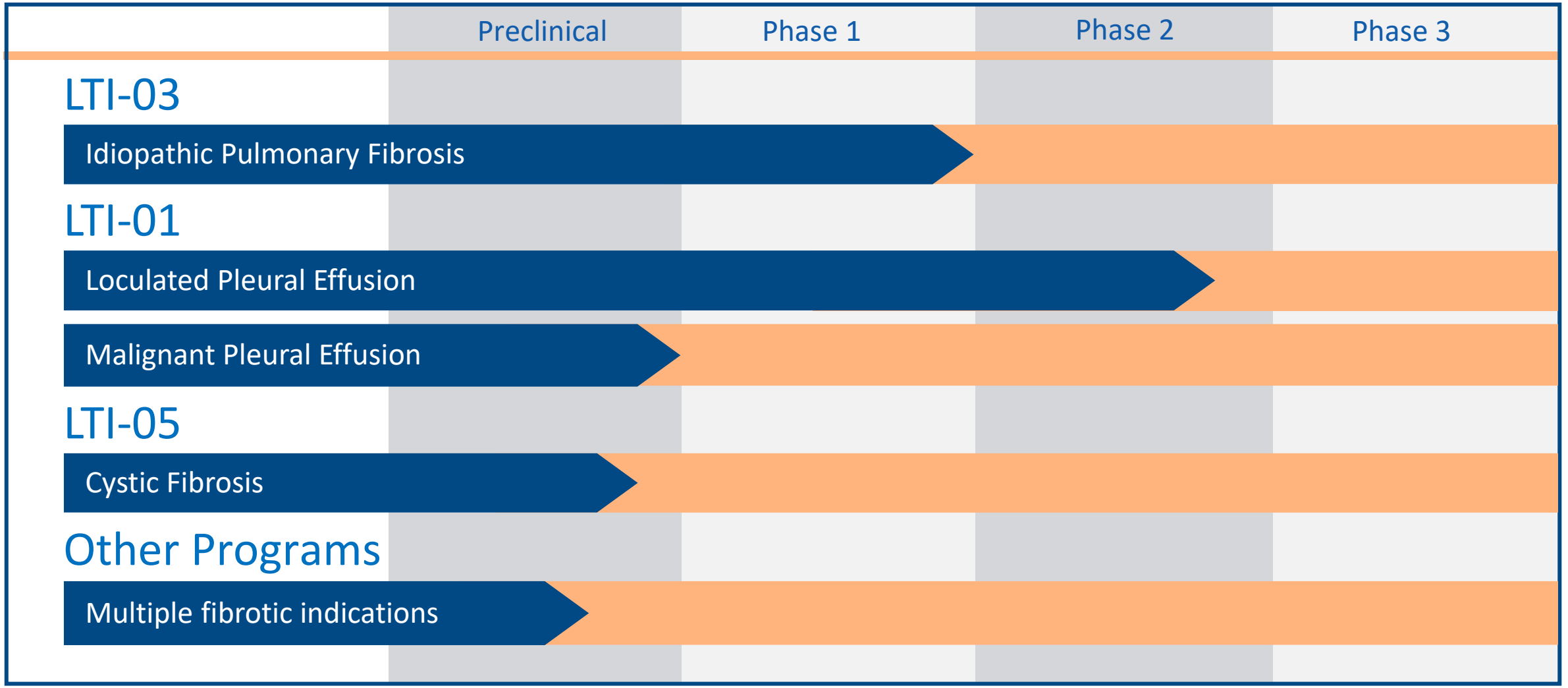
Multiple Orphan Disease Programs Ready for Phase 2 Clinical Trials



Led by Experienced Biotech and Pulmonary Team

Management and Board of Directors

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

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

Tim Cunningham
Chief Financial Officer

Sydney Kruger
VP Clinical Operations

Joe von Rickenbach
Chairman

Bill Fairey
Director

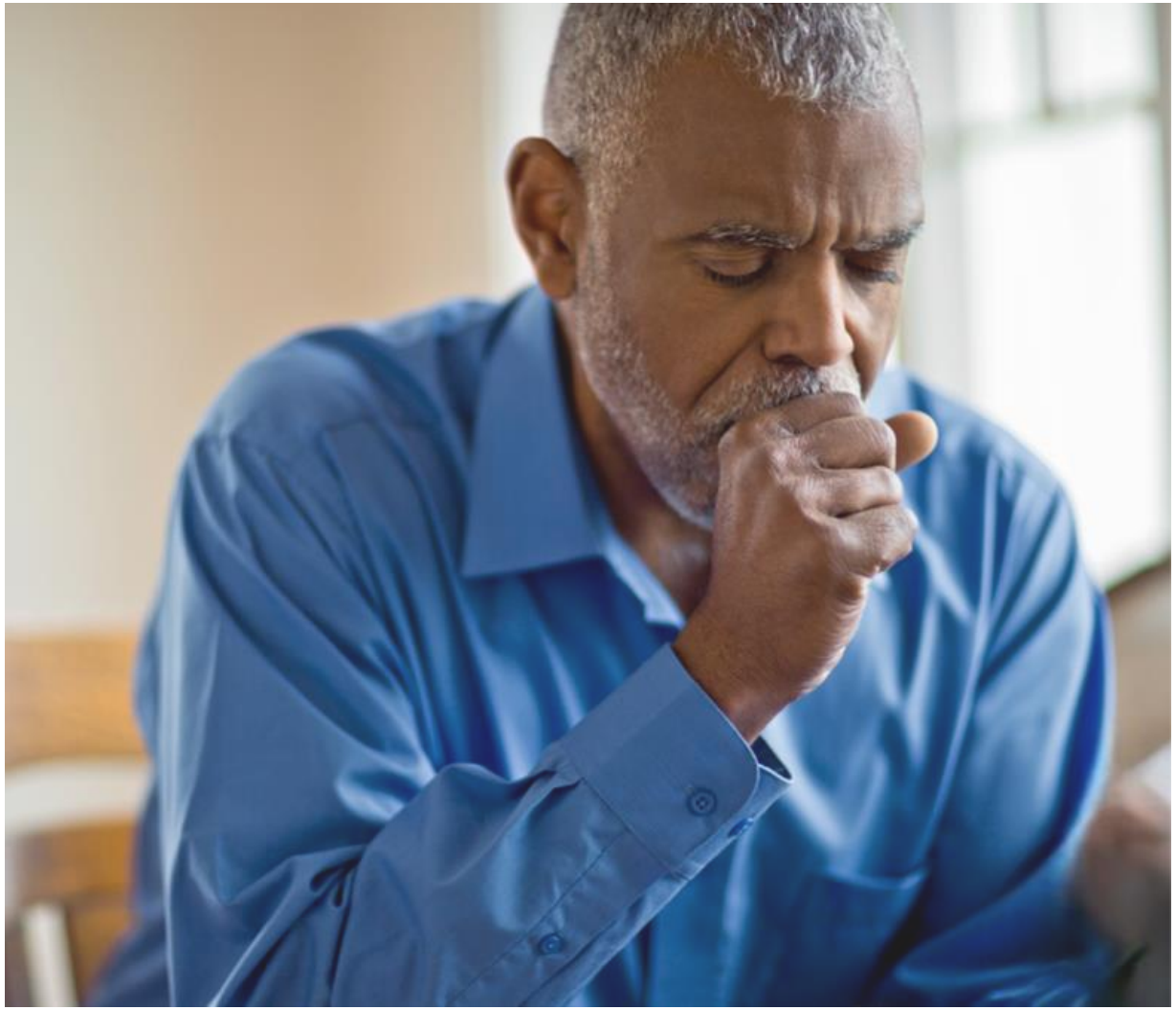
Alan Musso
Director

Reinhard Ambros, Ph.D.
Director

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]
- Approximately 100,000 patients in the US alone are living with IPF each year[3] and more than 250,000 Americans live with some sort of pulmonary fibrosis[2]
- Median survival from the time of diagnosis is 3-5 years



[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] https://www.healthline.com/health/managing-idiopathic-pulmonary-fibrosis/ipf-facts#prevalence
[4] Kirby, Living with idiopathic pulmonary fibrosis, The Lancet VOLUME 9, ISSUE 2, P136-138, FEBRUARY 2021

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Sizable Global Opportunity with Potential Upside

- Only 2 drugs are approved for IPF as of 2025
- Ofev®, the global leader, did more than $3.6B in sales for 2023[1]
- The estimated global market for IPF alone is projected to be $11.7B[2]
- Other PF and ILDs represent upside for a successful IPF drug
- The mechanism of LTI-03 could potentially address other fibrosis conditions, such as those associated with the heart, kidneys, liver, skin, or eyes

[1]https://www.boehringer-ingelheim.com/about-us/corporate-profile/boehringer-ingelheim-strong-growth-pipeline-acceleration-2023#:~:text=Human%20Pharma%20portfolio%20shows%20strong,more%20than%201%20billion%20people.

[2] iHealthcareAnalyst Global Idiopathic Pulmonary Fibrosis Market $11.7 Billion by 2031 January 5, 2024 by iHealthcareAnalyst, Inc. https://www.ihealthcareanalyst.com/global-idiopathic-pulmonary-fibrosistreatment-market/

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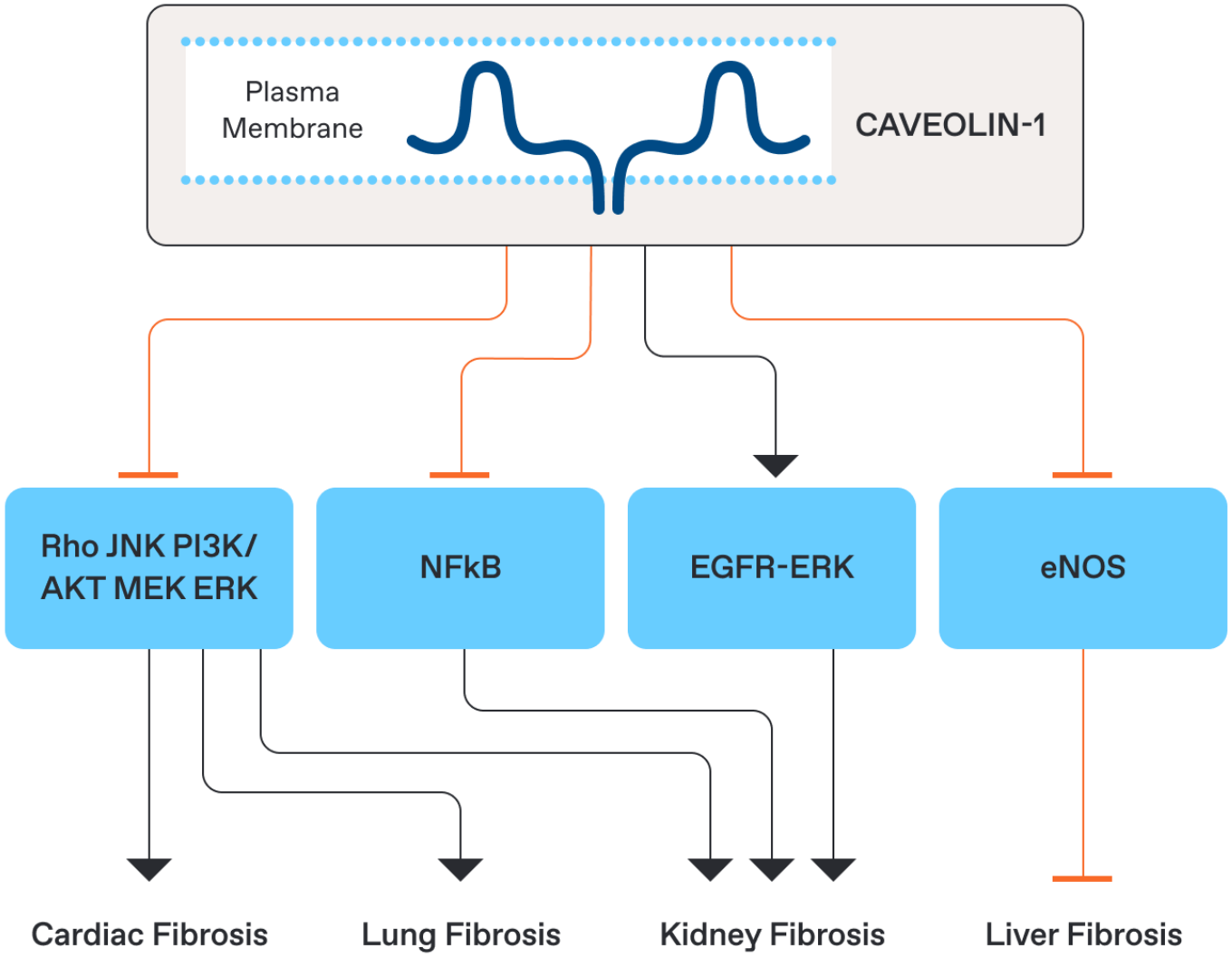
Caveolin-1 Regulates Proteins Involved in Multiple Fibrosis-Related Pathways in the Lung and Other Organs

- 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

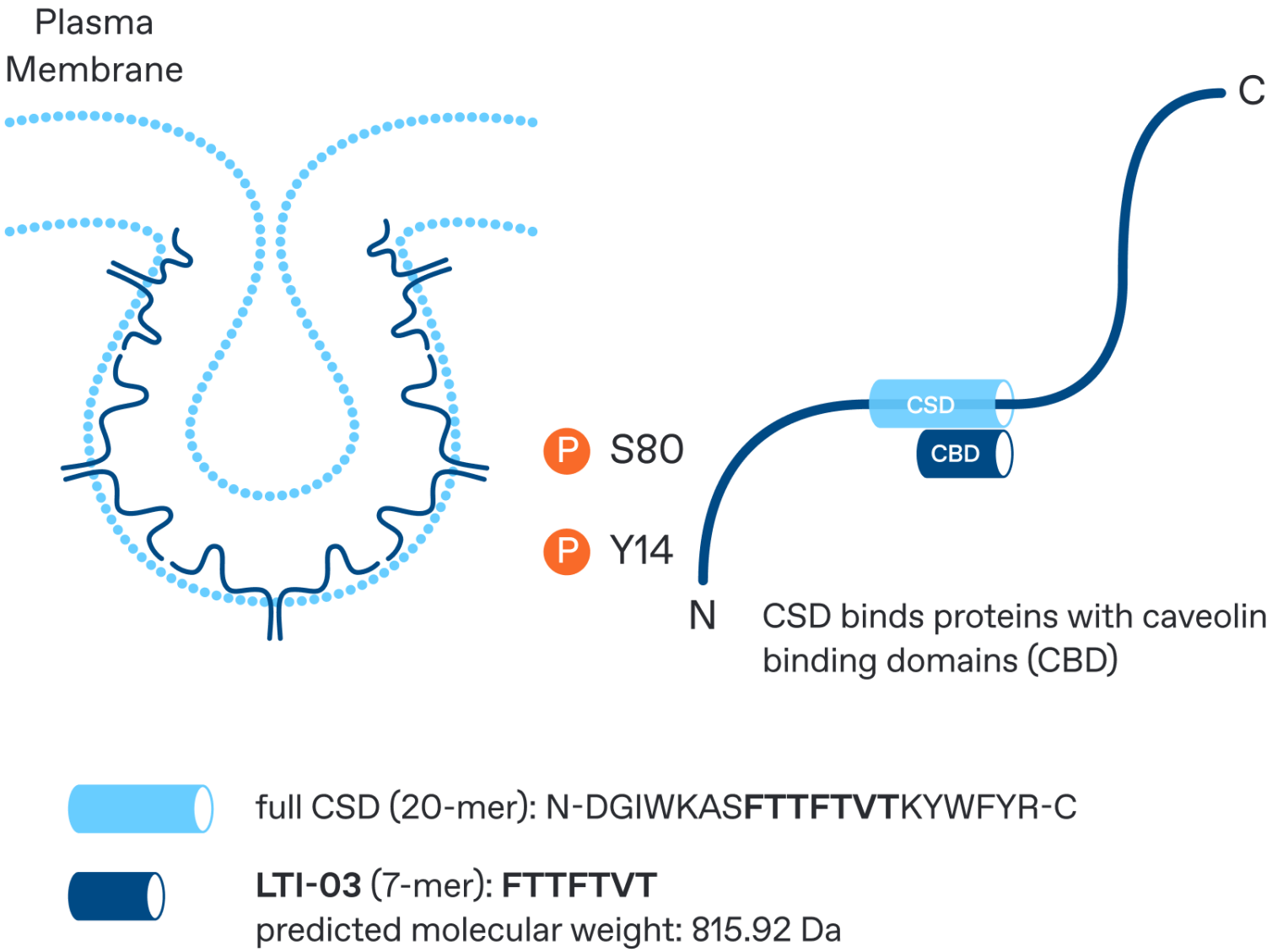


[1]Wang XM et al. Caveolin-1: a critical regulator of lung fibrosis in idiopathic pulmonary fibrosis. J Exp Med. 2006 Dec 25;203(13):2895-906.

Adapted from Gvaramia et al, Matrix Biology, 2013

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

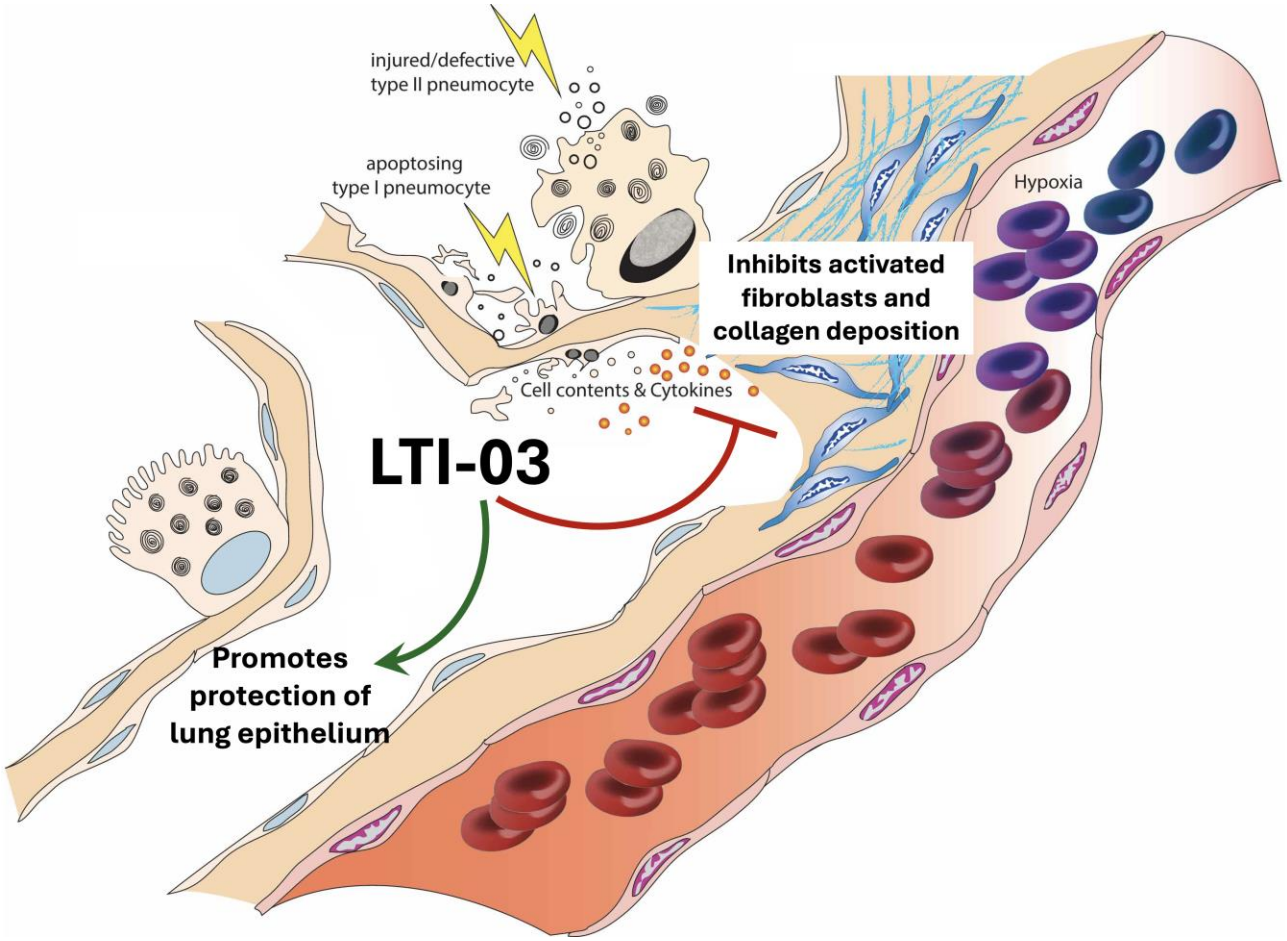
- LTI-03 is a seven amino acid peptide comprising a portion of the Cav1 CSD. Substitution/deletion analysis revealed it is the smallest CSD fragment that retains functionality
- This hydrophobic peptide can enter cells, and it may be acting both at the cell membrane and intracellularly
- Studies have 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

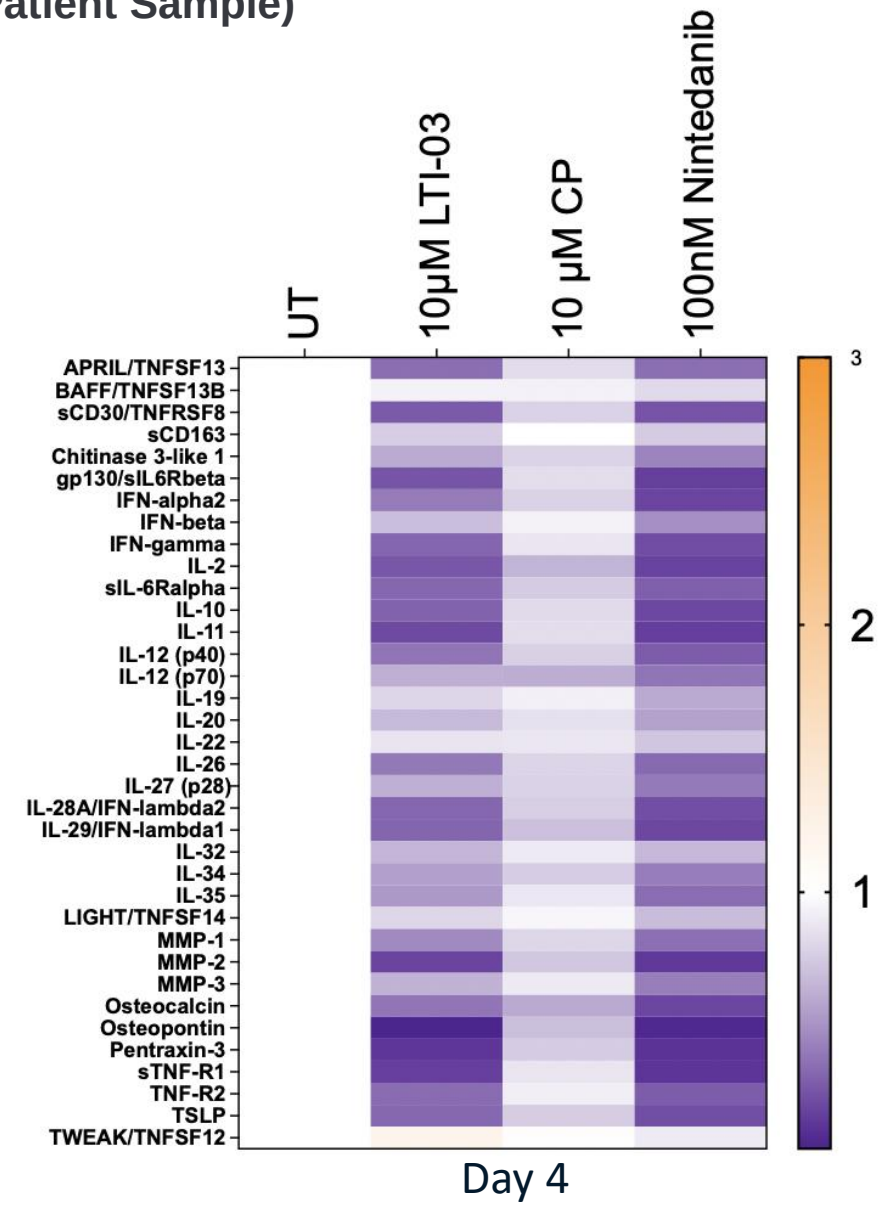
LTI-03's Dual Mechanism: Potent Antifibrotic Activity Combined with Epithelial Protection

- Other drugs act strictly as an antifibrotic, only addressing the lung scarring, and ultimately only slowing the progression of the disease
- LTI-03 acts to both inhibit profibrotic activity and to preserve epithelial progenitor cells, allowing for potential lung regeneration and restoration
- LTI-03 works to impact multiple fibrosis pathways—this multi-pathway approach is critical for better therapy



Antifibrotic Activity: Single dose LTI-03 inhibits multiple profibrotic proteins similar to Ofev®
(Every 12hrs in Precision Cut Lung Slices (PCLS)—Single Patient Sample)

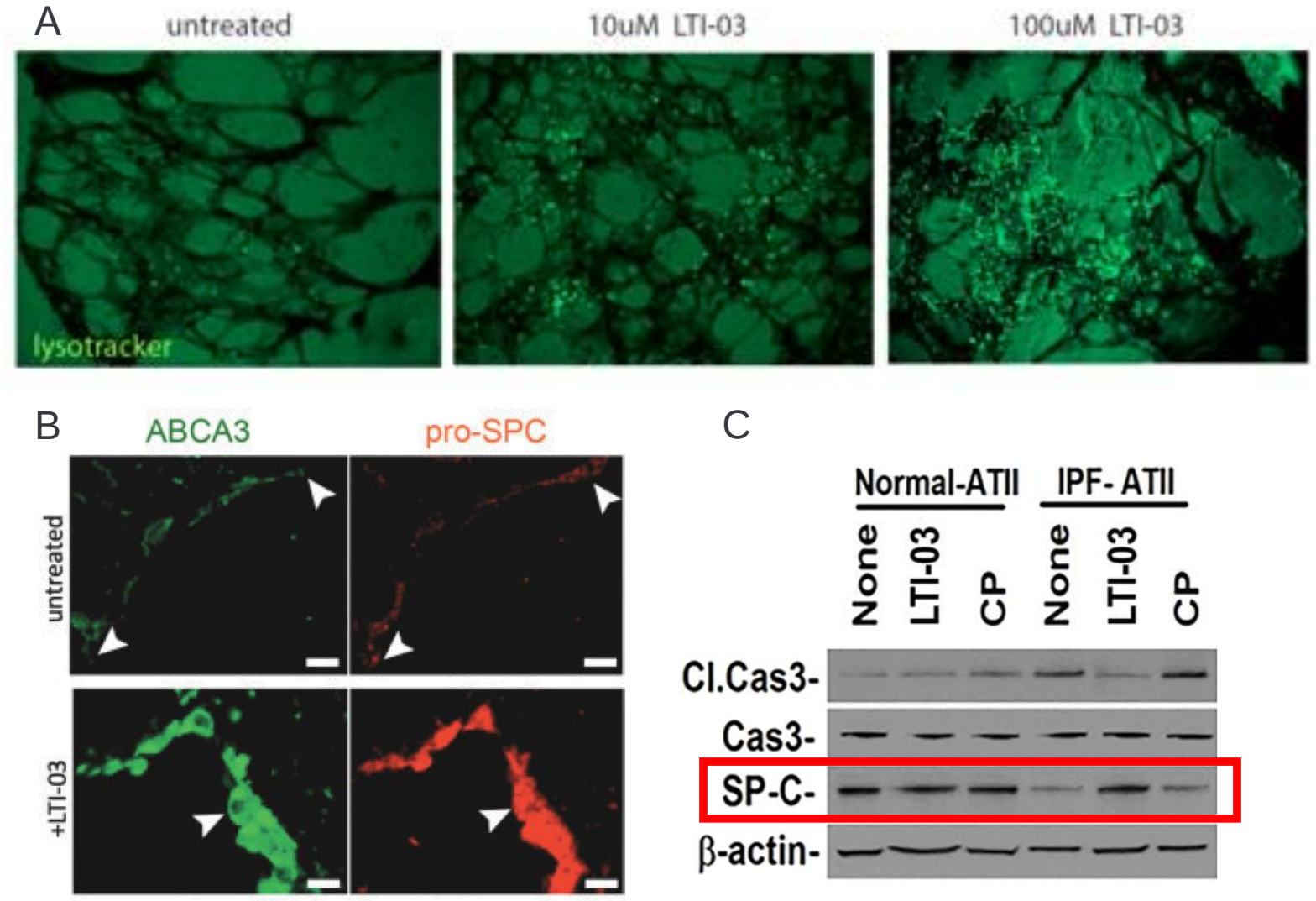
- As an **antifibrotic**, LTI-03 inhibits large panels of profibrotic proteins in a manner similar to the standard of care drug Ofev® (nintedanib)
  - Darker purple = more inhibition of the protein
- The PCLS tissue culture system uses actual biopsied tissue from an IPF lung (removed due to lung transplant), 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
- The equivalent human dose of 100nM nintedanib is very poorly tolerated, with significant GI side effects



Regenerative Activity: LTI-03 Preserves Critical Progenitor Cells in the Lung

(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



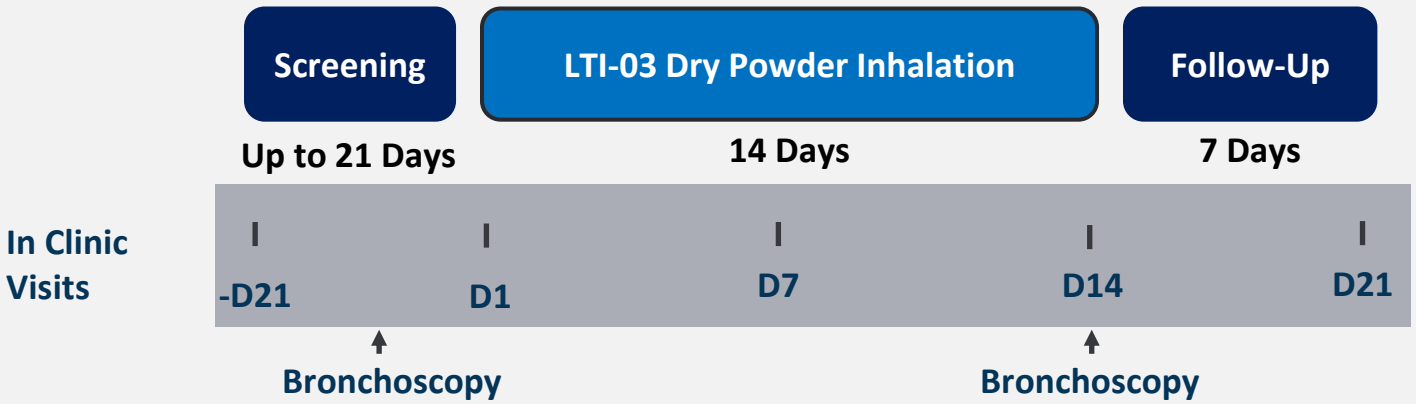
LTI-03: Clinical Evidence of Safety and Potential for Efficacy

Phase 1a Clinical Trial Design—At 20 mg and Below, LTI-03 is Safe and Well-Tolerated (Status: Complete)

Healthy Human Volunteer Clinical Trial

- Objectives
  - Primary – Safety and Tolerability
  - Secondary – Pharmacokinetics
- Design
  - Single Ascending Dose (32 subjects / 3 doses)
    - Doses: 20mg, 40mg, 80mg
  - Multiple Ascending Dose (40 subjects / 5 doses)
    - Doses: 2.5mg, 5mg, 10mg, 20mg, 40mg

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



Study Design

- IPF diagnosis ≤ 3 years; no previous antifibrotic therapy w/in 2 months of baseline
- 24 patients total (18 active, 6 placebo)
  - Low (2.5mg BID) and high (5mg BID) dose cohorts, sequential daily dosing for 14 days
- Bronchoscopy at screening and Day 14
- Primary endpoint: Safety/tolerability
- Key exploratory endpoints: Biomarkers (blood, BAL, brushings)

Robust Biomarker Evaluation for De-Risking of LTI-03
Several Markers Linked to Lung Function

- All of the biomarkers selected for evaluation
  - ✓ Have literature suggesting their involvement
  - ✓ Are primarily found in important cell types in the IPF lung
  - ✓ Were shown in preclinical studies to be attenuated by LTI-03
- Attenuation of markers in the Phase 1b trial would demonstrate
  - ✓ That LTI-03 is reaching important cells in the deeply fibrosed lung
  - ✓ Surrogate target engagement
  - ✓ That LTI-03 is positively affecting pathogenic factors in the IPF lung

Statistically Significant Biomarkers from Phase 1b Trial	
Associated with Fibroblasts/myofibroblasts cell-type	
Interleukin 11 (IL-11)	A predictor of prognosis and acute exacerbation in IPF patients
CXCL7	Proinflammatory and pro-fibrotic chemokine
Associated with Basal-like cell-type	
Thymic Stromal Lymphopoietin Protein (TSLP)	Expressed in fibroblasts and basal like epithelium of IPF UIP lesions
Galectin 7 (Gal7)	Highly expressed in Caveolin-1 deficient bronchiolized areas in the IPF lung

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IL-11 and Gal7: Strong Evidence of LTI-03 Activity and Potential

A. Gal7 is not expressed in normal lungs but highly expressed in IPF**

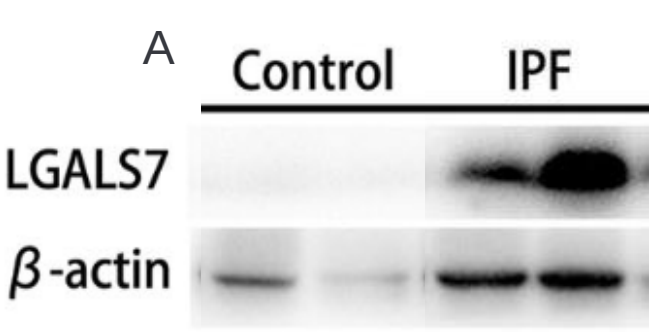
B. LTI-03 reduced Gal7 in preclinical work (SOC drugs did not)

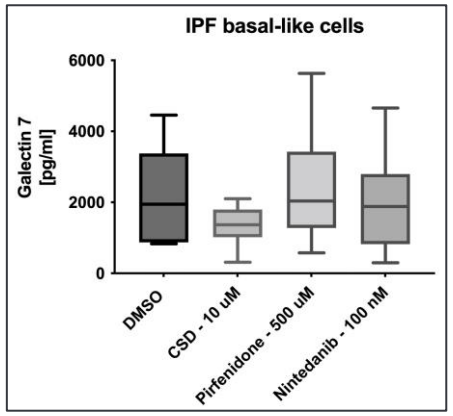
C. LTI-03 significantly reduced Gal7 in IPF patients (vs placebo)

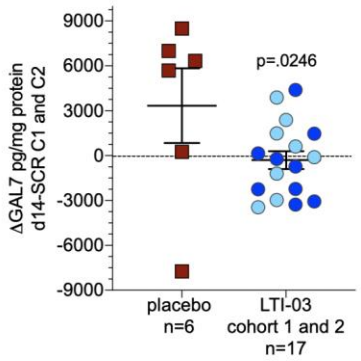
D. IL-11 is highly expressed in IPF*

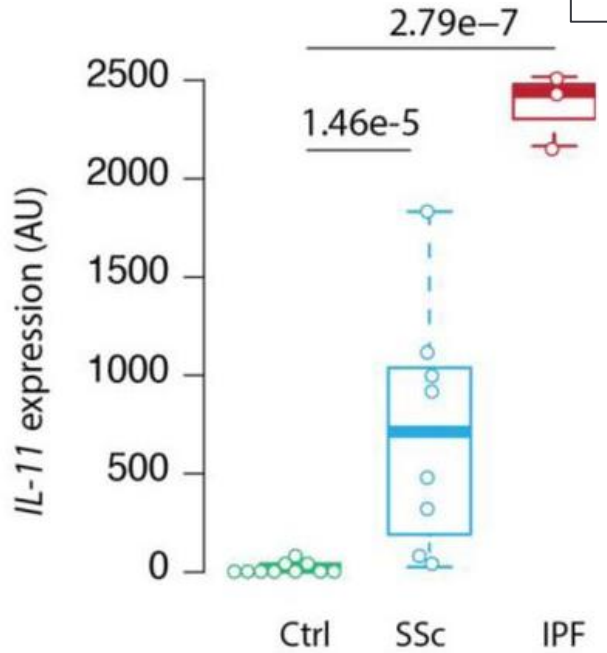
E. LTI-03 significantly reduced IL-11 in IPF patients (vs placebo)

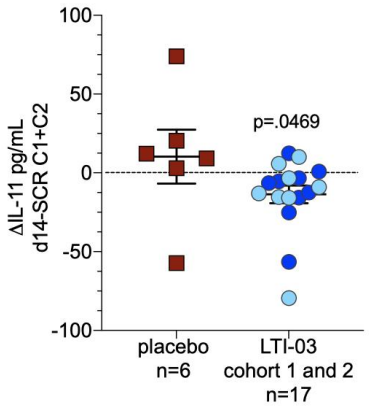
F. IL-11 is a predictor of prognosis and acute exacerbation in IPF patients*











F

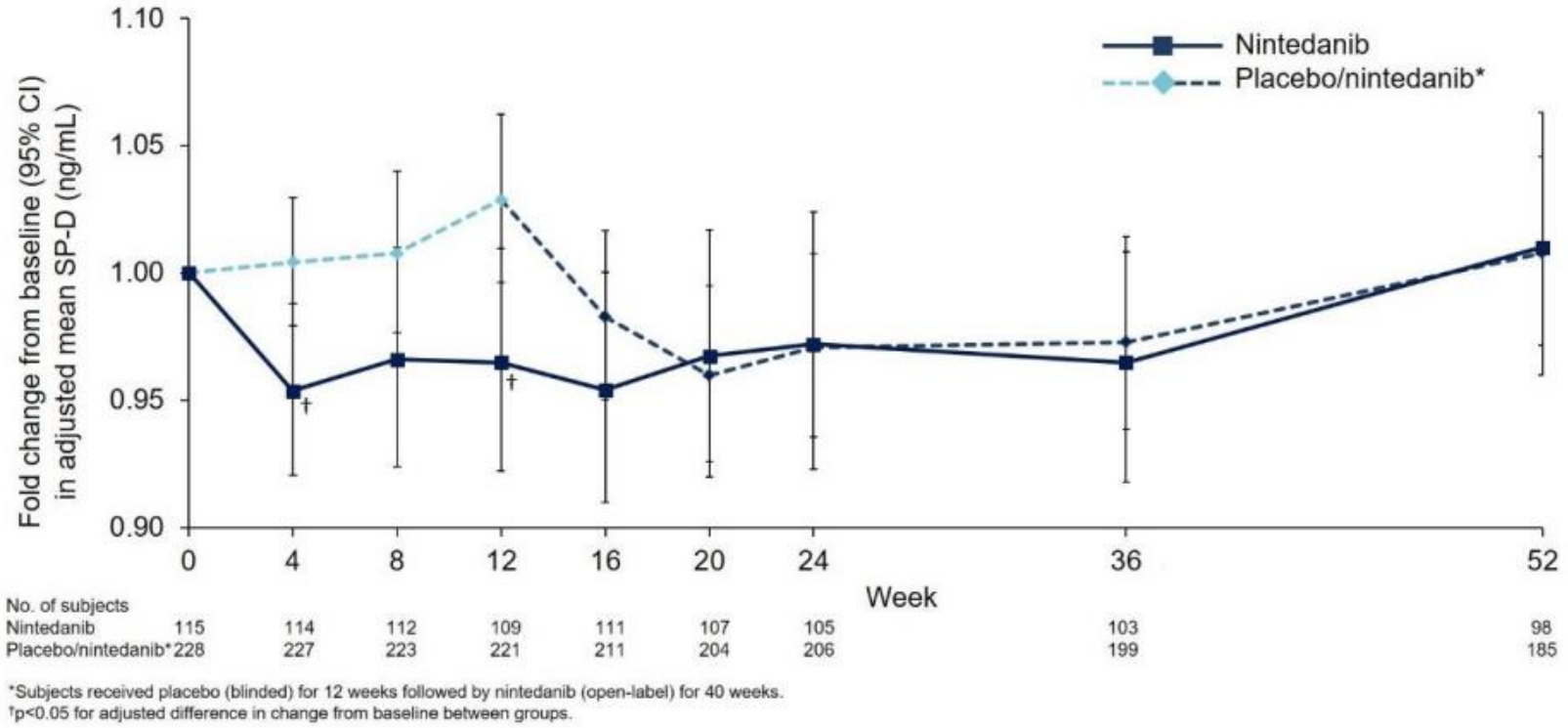
IPF and investigated its predictive significance for survival and AE occurrence. The serum IL-11/%FVC value was an independent predictor of prognosis and AE occurrence in patients with IPF, and the IL-11 level appeared to show pathophysiologic value in IPF.

*Arai T, Hirose M, Kagawa T, Hatsuda K, Inoue Y. Interleukin-11 in idiopathic pulmonary fibrosis: predictive value of prognosis and acute exacerbation. J Thorac Dis. 2023 Feb 28;15(2):300-310.

**Tian Y, Li H, Gao Y, Liu C, Qiu T, Wu H, Cao M, Zhang Y, Ding H, Chen J, Cai H. Quantitative proteomic characterization of lung tissue in idiopathic pulmonary fibrosis. Clin Proteomics. 2019 Feb 6;16:6.

Surfactant Protein D (SPD) is an important biomarker for the approved IPF drug Ofev®* and Now for LTI-03

- 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 (5 mg BID) decreased SPD by 5% over two weeks in the Phase 1b trial



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; in press

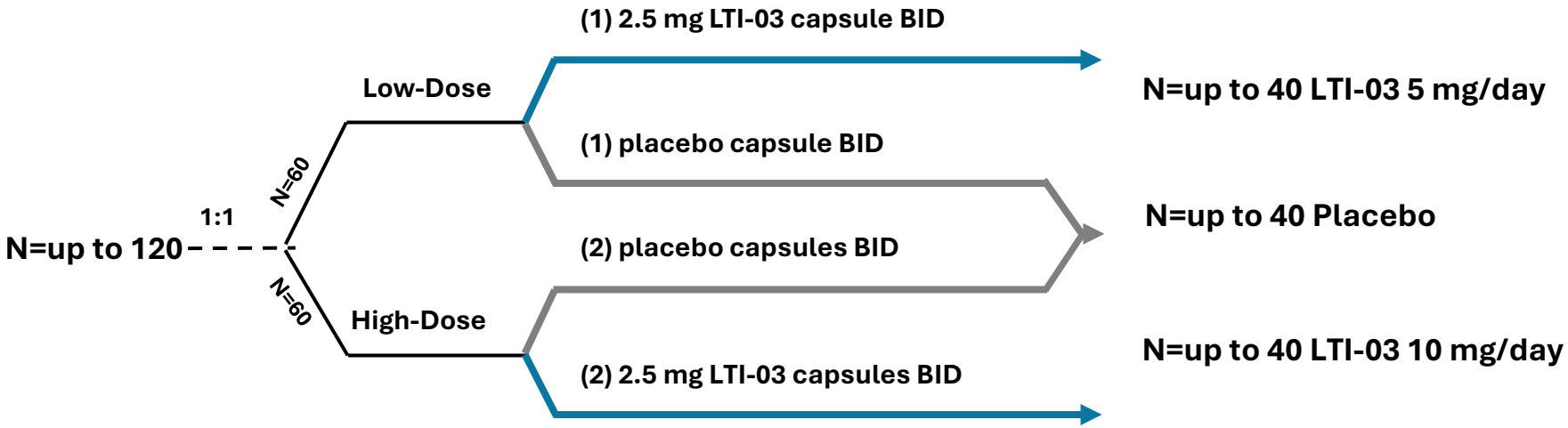
LTI-03 Next Steps – Phase 2 Study Measuring Lung Function

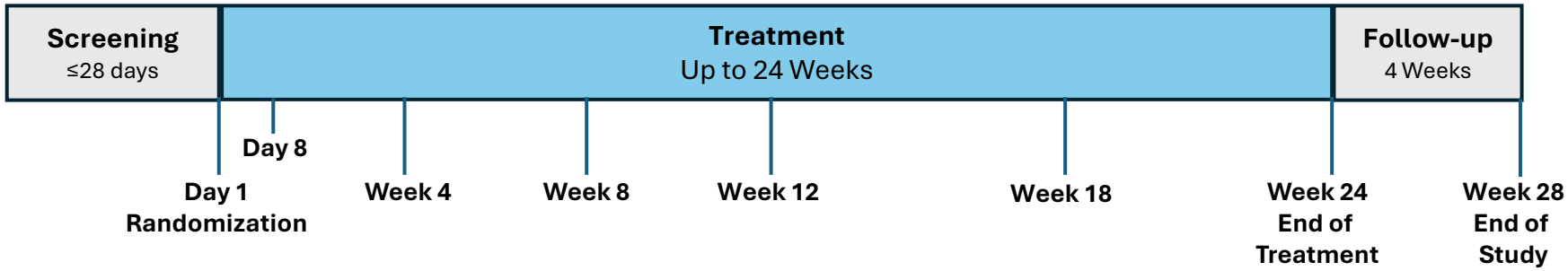
Primary endpoints

Safety and tolerability measured by incidence of treatment emergent adverse events

Efficacy of inhaled LTI-03 measured by:

- Change from baseline in FVC in mL
- Change from baseline in percent predicted FVC
- Change from baseline in lung fibrosis measure by HRCT



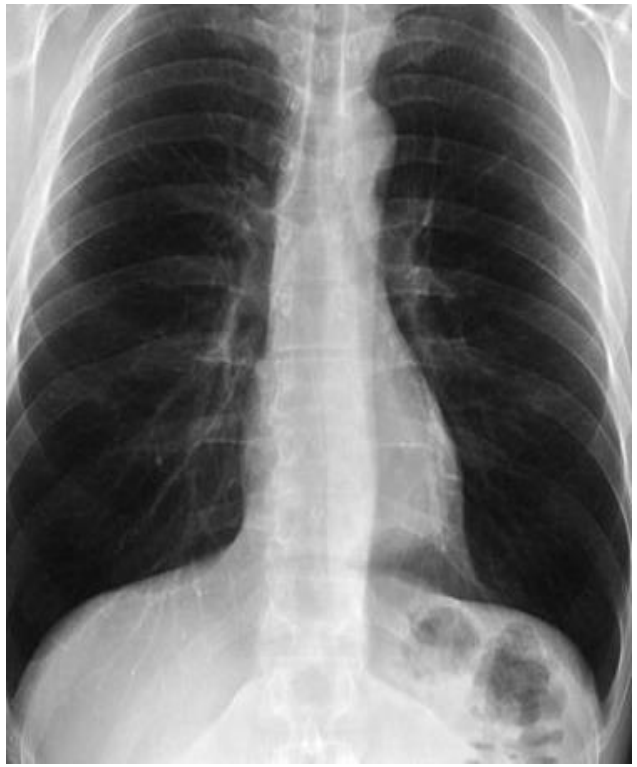


LTI-01: the First Drug Developed for Loculated Pleural Effusion

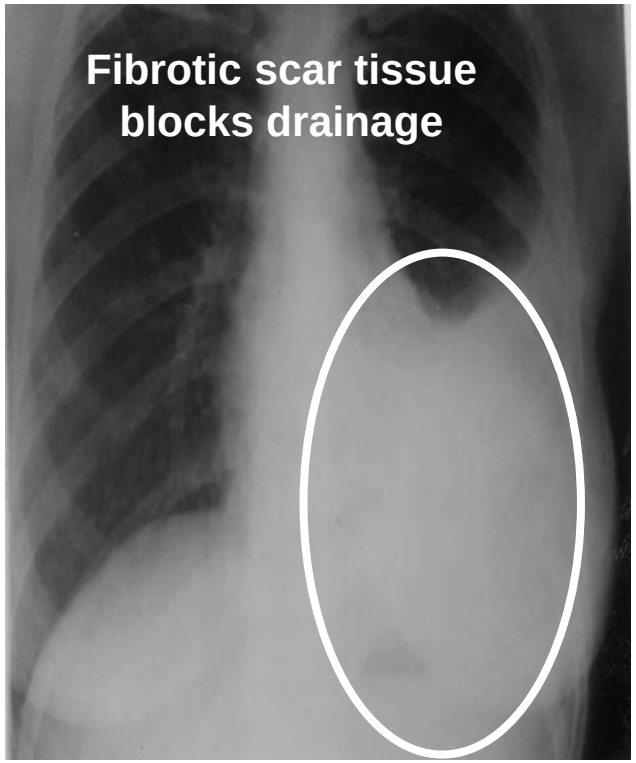
There Are No Approved Drug Treatments for Loculated Pleural Effusion

- Loculated pleural effusion, or LPE occurs when fibrotic scar tissue forms in the pleural cavity, preventing effective drainage of fluid
- LPE is a frequent pneumonia complication in the elderly with a ~20% mortality rate
- LPE is managed with tPA/DNase (off-label) and/or surgery (costly and invasive)
- Surgery can be effective but can also result in lengthy hospital stays. This is why off-label fibrinolytics is widely regarded as first line therapy
- Off-label therapy
  - Not FDA approved for LPE
  - Risk of intrapleural hemorrhage
  - Problematic dosing (at least twice daily, 12 hours apart)

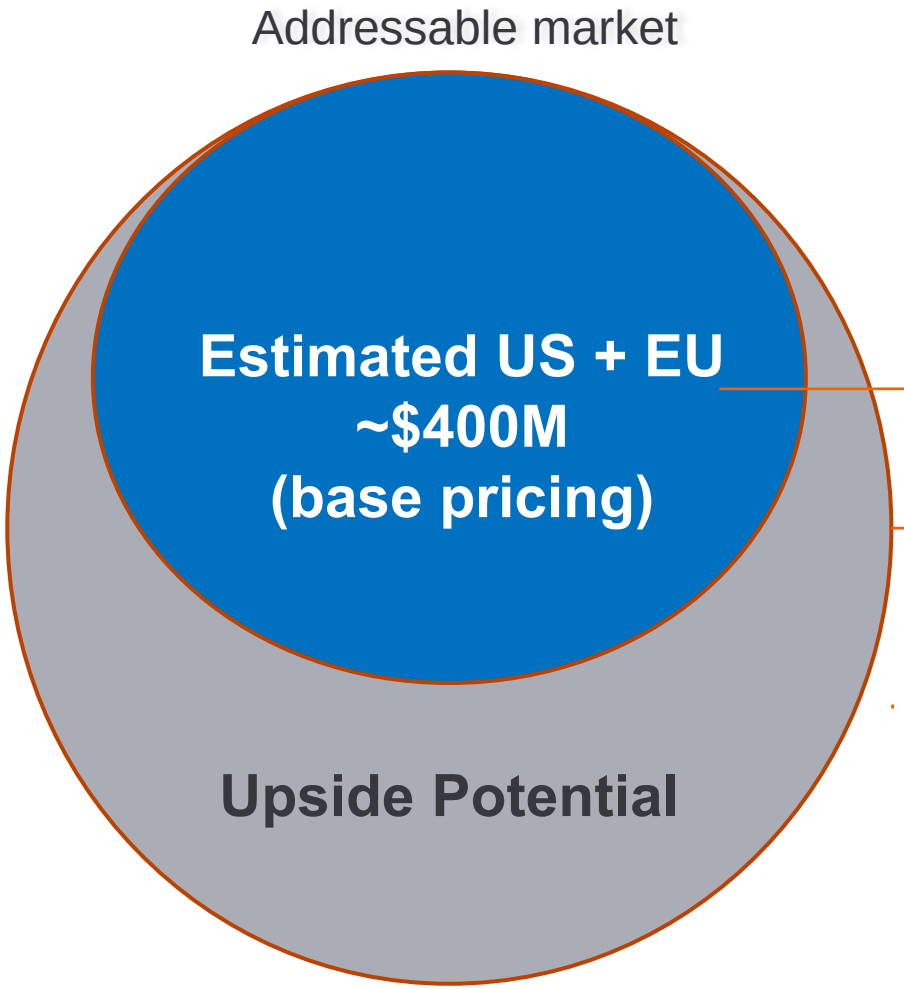
Healthy Lungs



Loculated Pleural Effusion



Sizeable US and EU Commercial Opportunity with Potential Upside



+ Japan partnership with TAIHO PHARMA

Current US and EU Opportunity

- 30,000 US fibrinolytic patients
- Up to 30,000 additional US LPE patients
- tPA/DNase priced at $6,700 per patient in US
- Estimate similar EU market opportunity to US market

Key Catalyst: Substitution of tPA/DNase with on-label therapeutic

Upside Market Potential in the US and EU

- Premium Pricing
- Ability to drive beneficial clinical and economic outcomes

Key Catalyst: On-label therapy with clear efficacy, safety and dosing benefits

Source: Management estimates, industry publications and MME market access research study for Rein Tx

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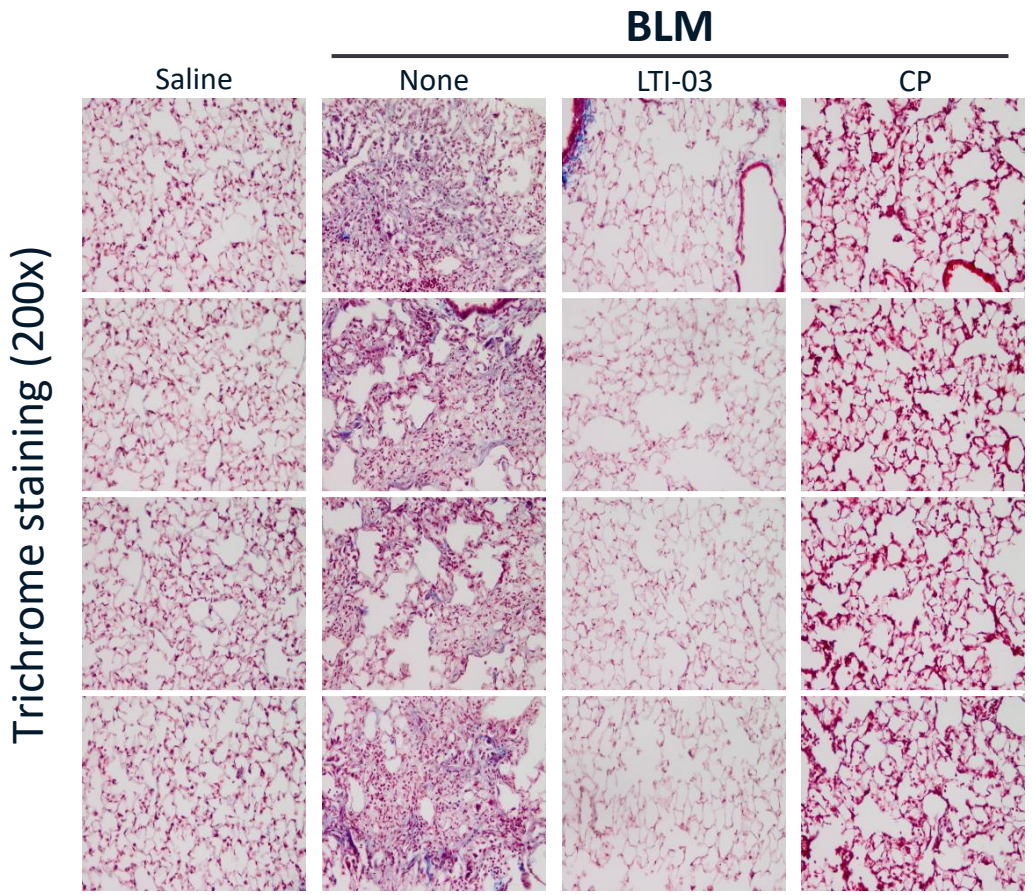
Nasdaq: RNTX

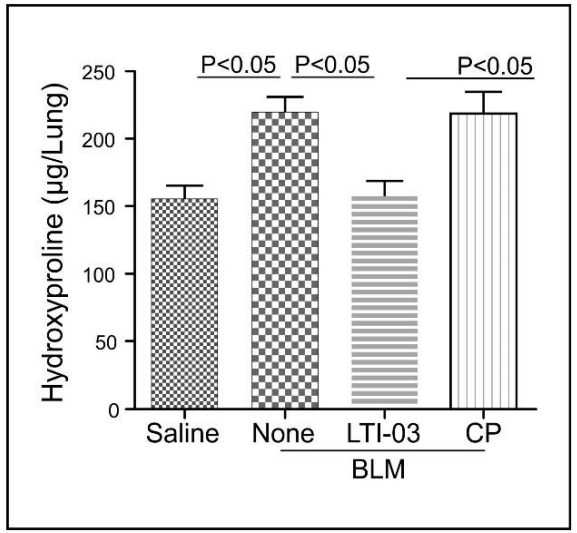
Appendix

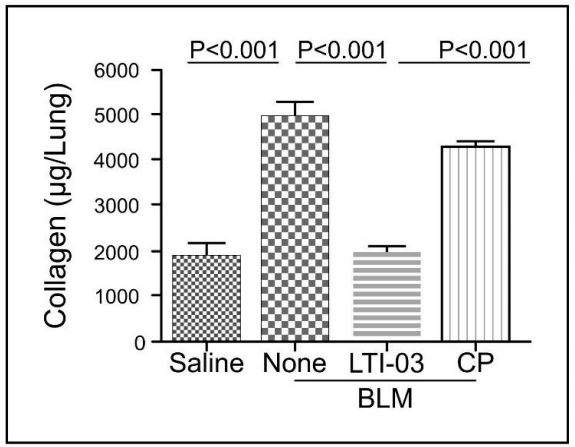
Demonstrated Anti-Fibrotic Properties in the 21-day Bleomycin Mouse Model of IPF



*The **bleomycin mouse model is an established murine model** for characterizing and assessing the impact of novel IPF therapies*

Fibrotic biomarkers





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

Cohort Two Biomarker Results

Biomarker	Positive Trend C2	Statistically Significant (p<0.05) C2	Positive Trend C1+C2	Statistically Significant (p<0.05) C1+C2	dose dependency
Fibroblasts/ myofibroblasts					
COL1A1	✓		✓		✓
IL-11	✓		✓	✓	
CXCL7	✓	✓	✓	✓	✓
pSMAD/ tSMAD					
Basal-like cells					
TSLP	✓	✓	✓	✓	✓
GAL7	✓	✓	✓	✓	✓
Alveolar epithelial health					
SPD	✓		✓		✓
Inflammation/ safety					
%pAKT	✓	N/A	✓	N/A	N/A

Caveo

- Caveolin-1 (

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