Corporate Presentation

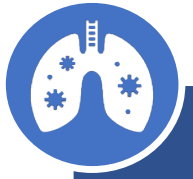
April 2024

Forward-Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements of Aileron Therapeutics, Inc. ("Aileron", the "Company", "we", "our" or "us") within the meaning of the Private Securities Litigation Reform Act of 1995, including statements with respect to: future expectations, plans and prospects for the Company; the milestones of the Company; the projected cash runway of the Company; the status and plans for clinical trials, including the timing of data; future product development; 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, 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. FDA 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; our potential dependence on collaboration partners; 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, which is on file with the Securities and Exchange Commission, and in subsequent filings that the Company files with the Securities and Exchange Commission. 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.

This presentation contains estimates and other statistical data made by independent parties and by us relating to our clinical data, market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

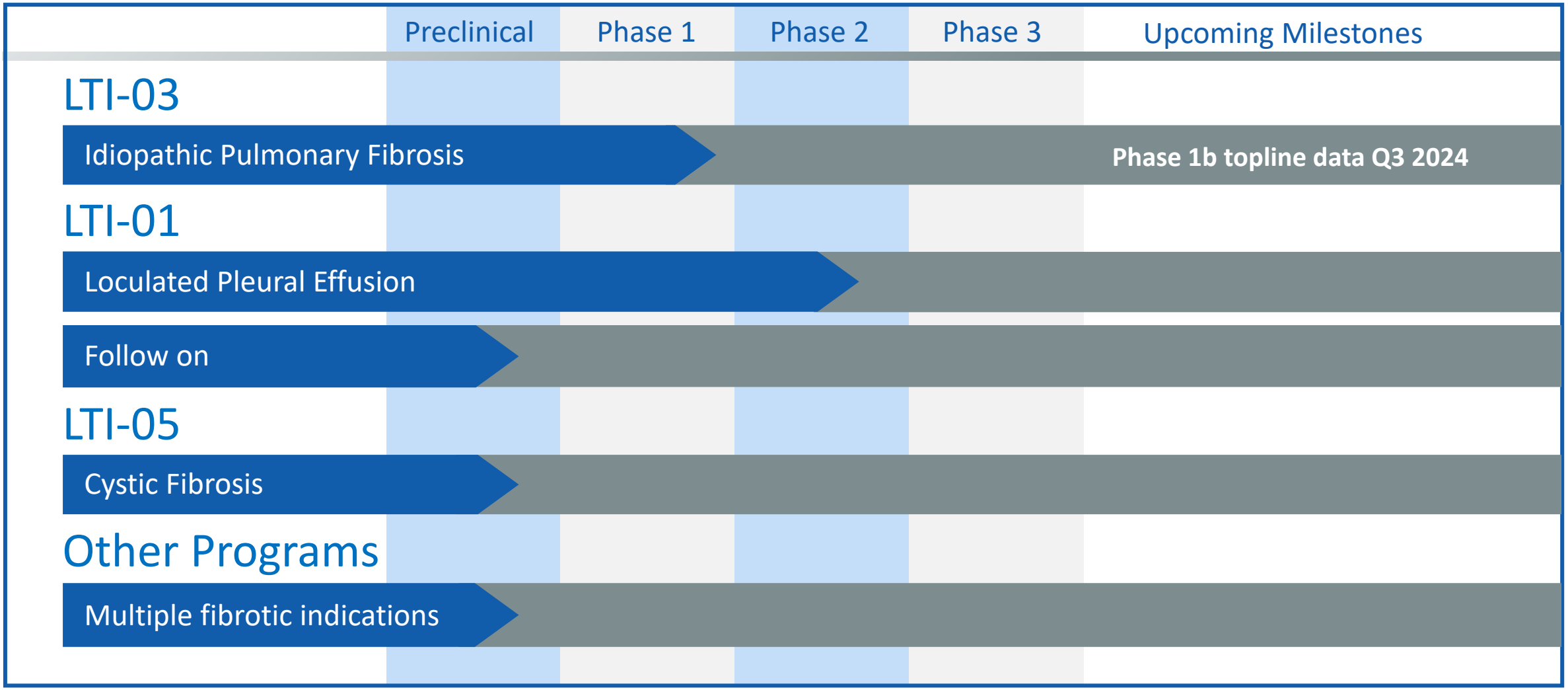
Clinical-stage Biotech with Pulmonary Pipeline



Therapies for Underserved Fibrosis and Pulmonary Conditions

LTI-03 ***Idiopathic Pulmonary Fibrosis***	***Phase 1b***	• Preclinical evidence supporting the ability to **protect healthy lung epithelial cells** and to **reduce pro-fibrotic signaling** • Demonstrated ability to increase sRAGE, a **prognostic biomarker** of IPF
LTI-01 ***Loculated Pleural Effusions***	***Phase 2b ready***	• **Potentially fatal disease** with no approved drugs • Completed Phase 1b and Phase 2a trials; similar mechanism to fibrinolytics used off label
LTI-05 ***Cystic Fibrosis***	***Lead Optimization***	• 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

Multiple Orphan Disease Programs with Upcoming Milestones



Led by an Experienced Biotech and Pulmonary Team

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TFF PHARMACEUTICALS · enavail · emergent

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Chief Scientific Officer (consulting)

Cedars Sinai

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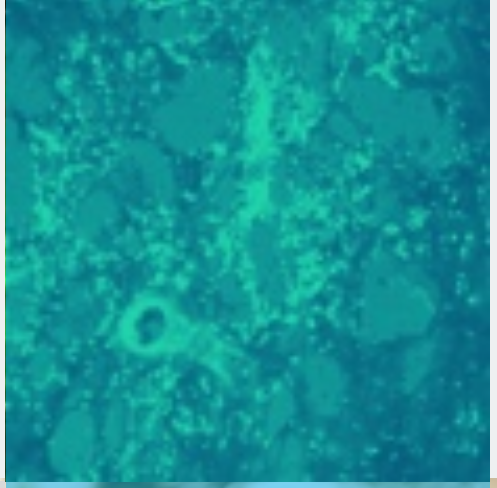
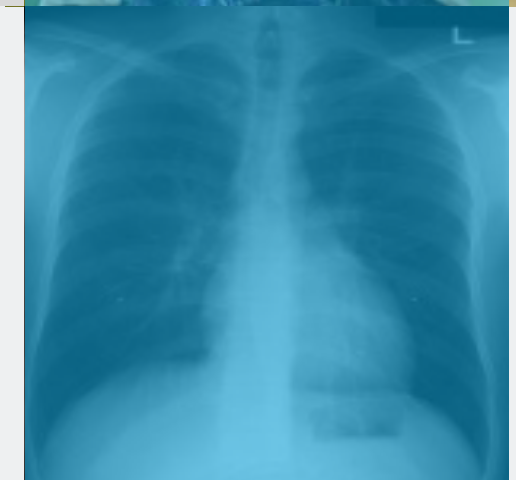
Director

Manuel Aivado, M.D., Ph.D.
Director

gsk · TAIHO PHARMA

LTI-03: A Novel Treatment for Idiopathic Pulmonary Fibrosis



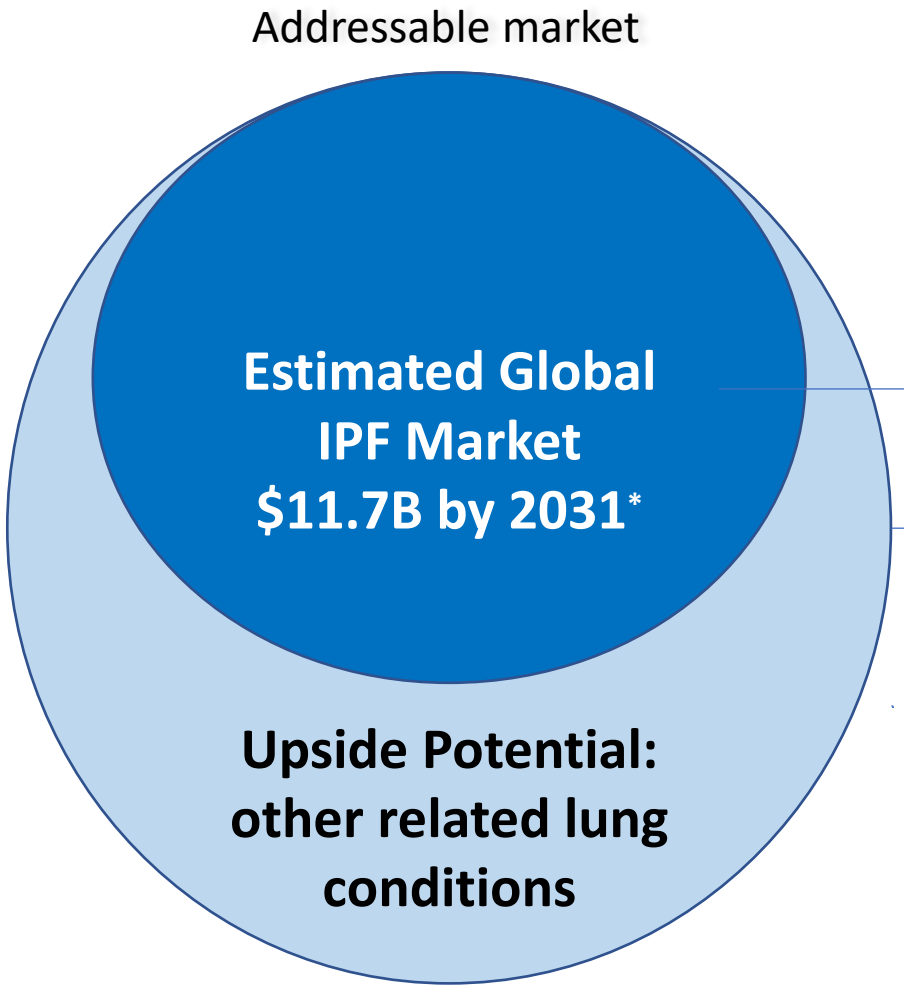


LTI-03 is a Peptide Region of Caveolin-1 Protein in Development for Idiopathic Pulmonary Fibrosis

- Multiple preclinical studies support dual mechanism of Cav1 – ability to inhibit multiple pro-fibrotic pathways and protect lung epithelial cells
- We believe current SOC treatment options offer modest clinical benefit, have significant side effects and intolerance, and are not curative
  - ~100,000[1] IPF patients in the U.S. with expected median survival 2-5 years[2] from diagnosis
- Completed Phase 1a randomized, double-blind placebo-controlled study in healthy normal volunteers
  - Currently in a Phase 1b randomized, double-blind placebo-controlled study
- sRAGE - prognostic biomarker of IPF disease preferentially increased in ex-vivo IPF tissue samples and Phase 1a treated patients
  - RAGE is primarily expressed by epithelial cells in lung tissue

1 United States National Library of Medicine website.
2 Nathan et al. Long-term Course and Prognosis of Idiopathic Pulmonary Fibrosis in the New Millennium. *Chest Journa*l Volume 140, ISSUE 1, P221-229, July 2011

Sizeable Global Opportunity in IPF with Potential Upside



Global Opportunity

- Affects 13 to 20 out of every 100,000 people worldwide**
- Only 2 drugs approved as of 2024
- Cost for Ofev oral capsule (100 mg) is approximately $13,695 for a supply of 60 capsules, depending on the pharmacy***

Upside Market Potential

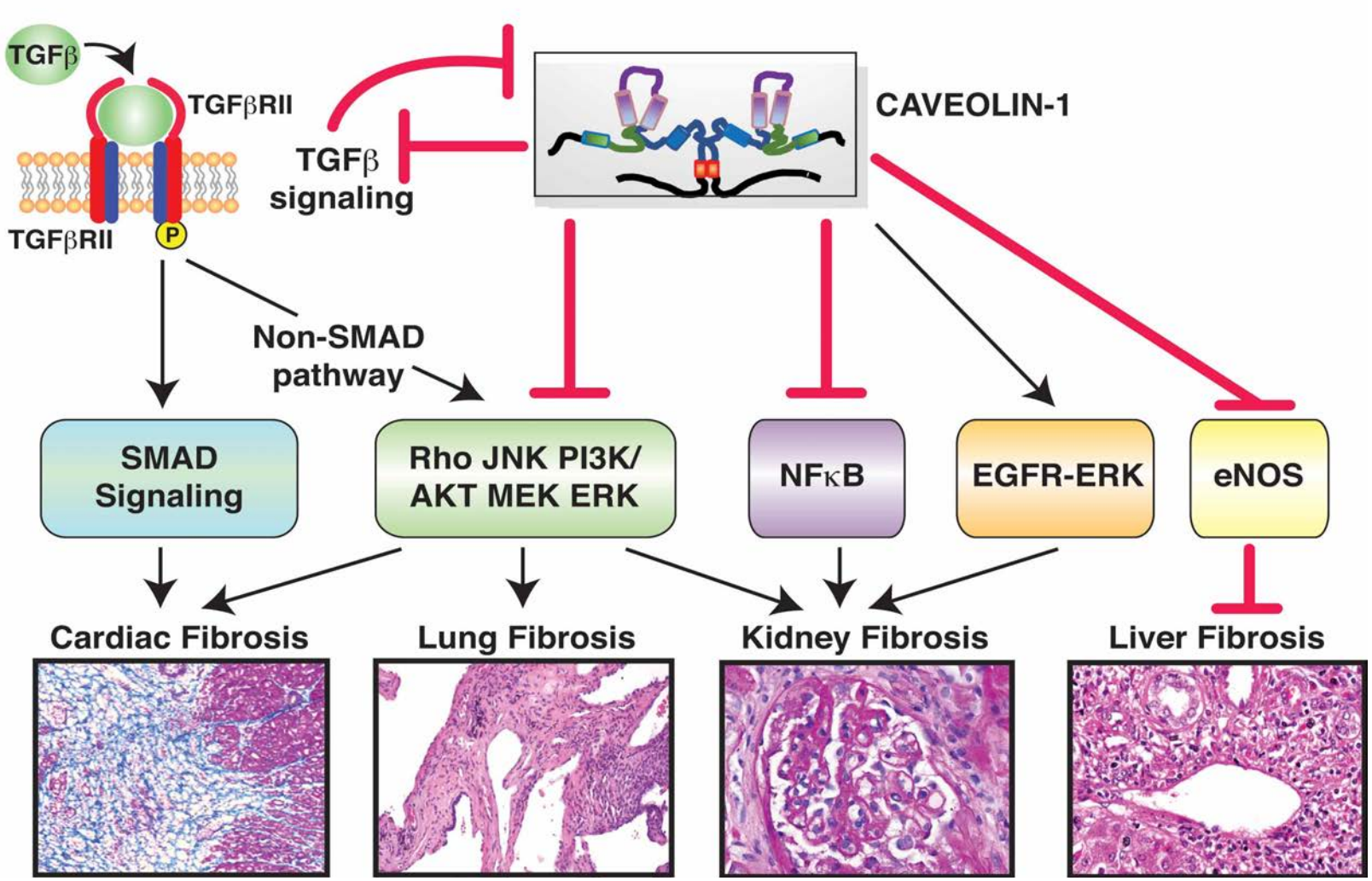
- Other interstitial lung diseases (ILDs)
- Possibly other lung conditions

*Source: iHealthcareAnalyst Global Idiopathic Pulmonary Fibrosis Market $11.7 Billion by 2031 January 5, 2024 by iHealthcareAnalyst, Inc. https://www.ihealthcareanalyst.com/global-idiopathic-pulmonary-fibrosis-treatment-market/

**Source: United States National Library of Medicine website. "Idiopathic Pulmonary Fibrosis," http://ghr.nlm.nih.gov/condition/idiopathic-pulmonary-fibrosis.

***Source: Drugs.com https://www.drugs.com/price-guide/ofev#

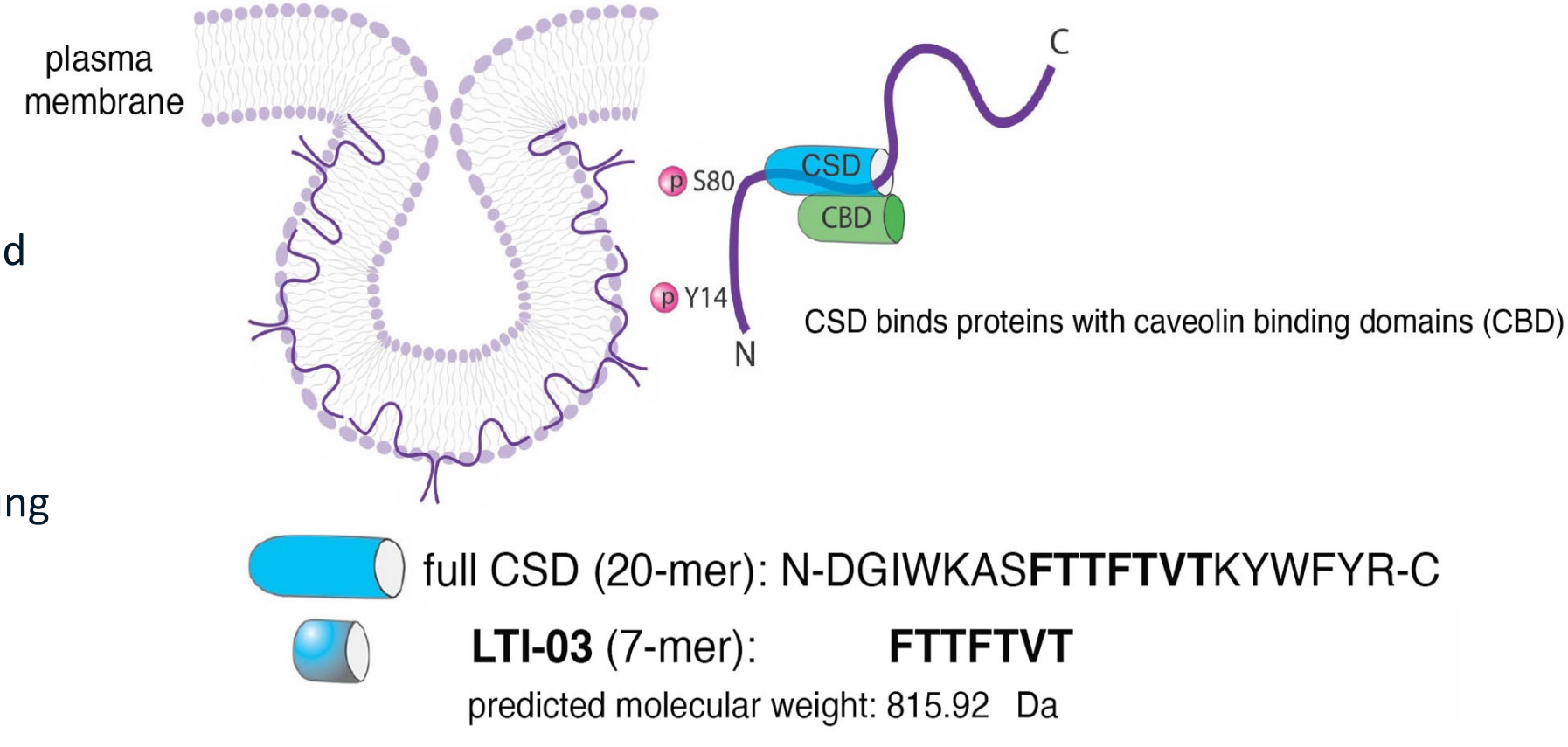
Caveolin-1 Modulates Multiple Fibrosis-Related Pathways



Adapted from Gvaramia et al, Matrix Biology, 2013

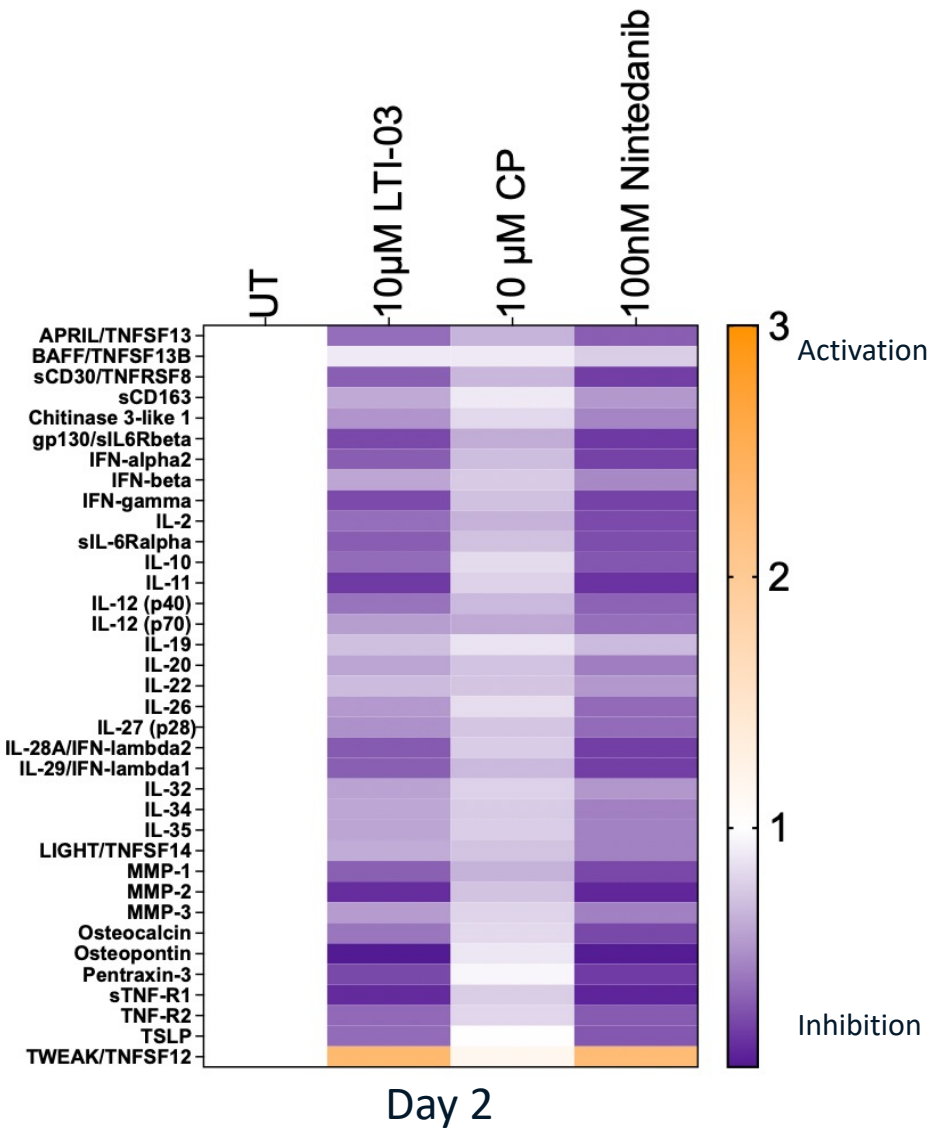
Simulation of Caveolin-1 Activity via CSD Peptide

- LTI-03 is a seven amino acid peptide encompassing a portion of the Cav1 CSD
- LTI-03 is dosed direct-to-lung by dry powder inhaler

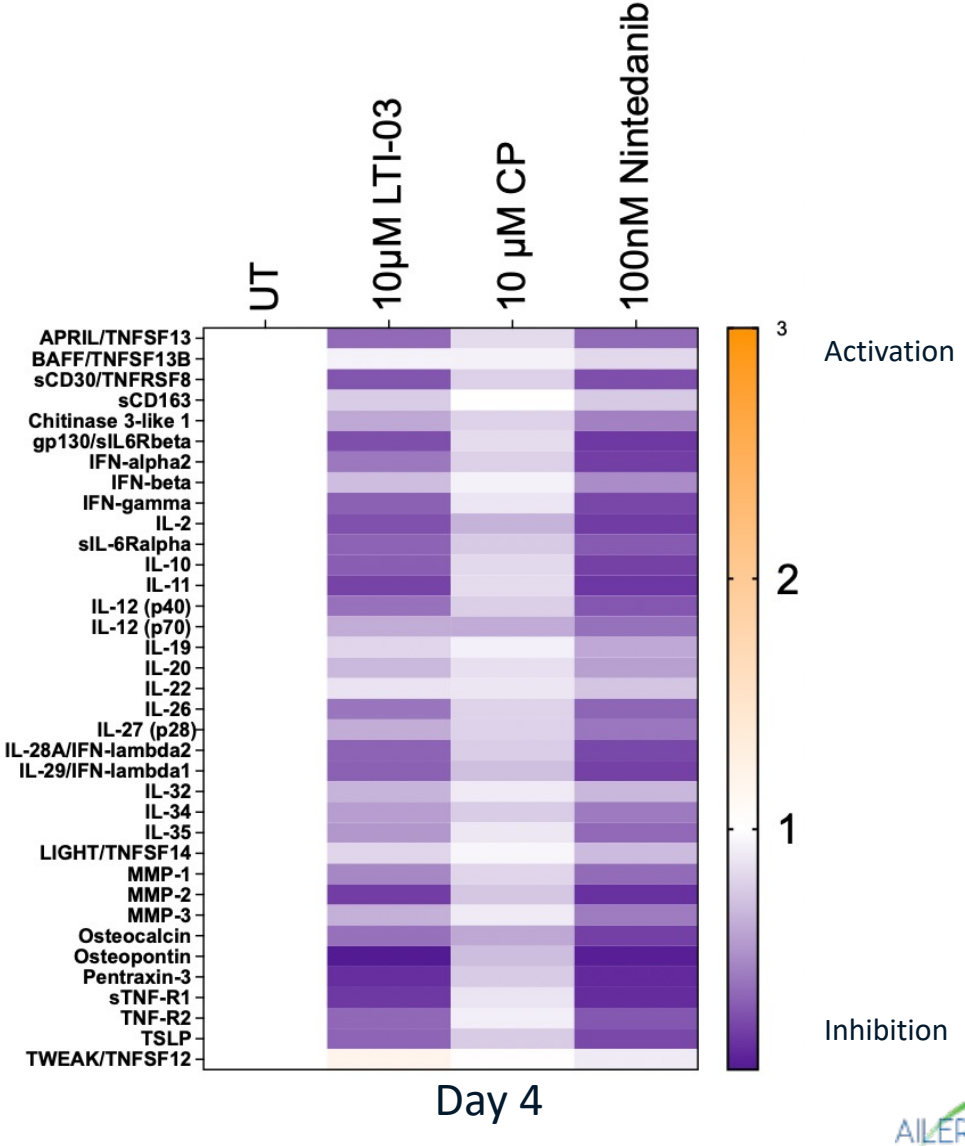


For a review on CSD/CBD binding domain list, see: Byrne et. al. PLOS One 2012

Anti-fibrotic Activity at Physiologically Relevant Dose (Every 12hrs in Precision Cut Lung Slices (PCLS)—Single Patient Sample)

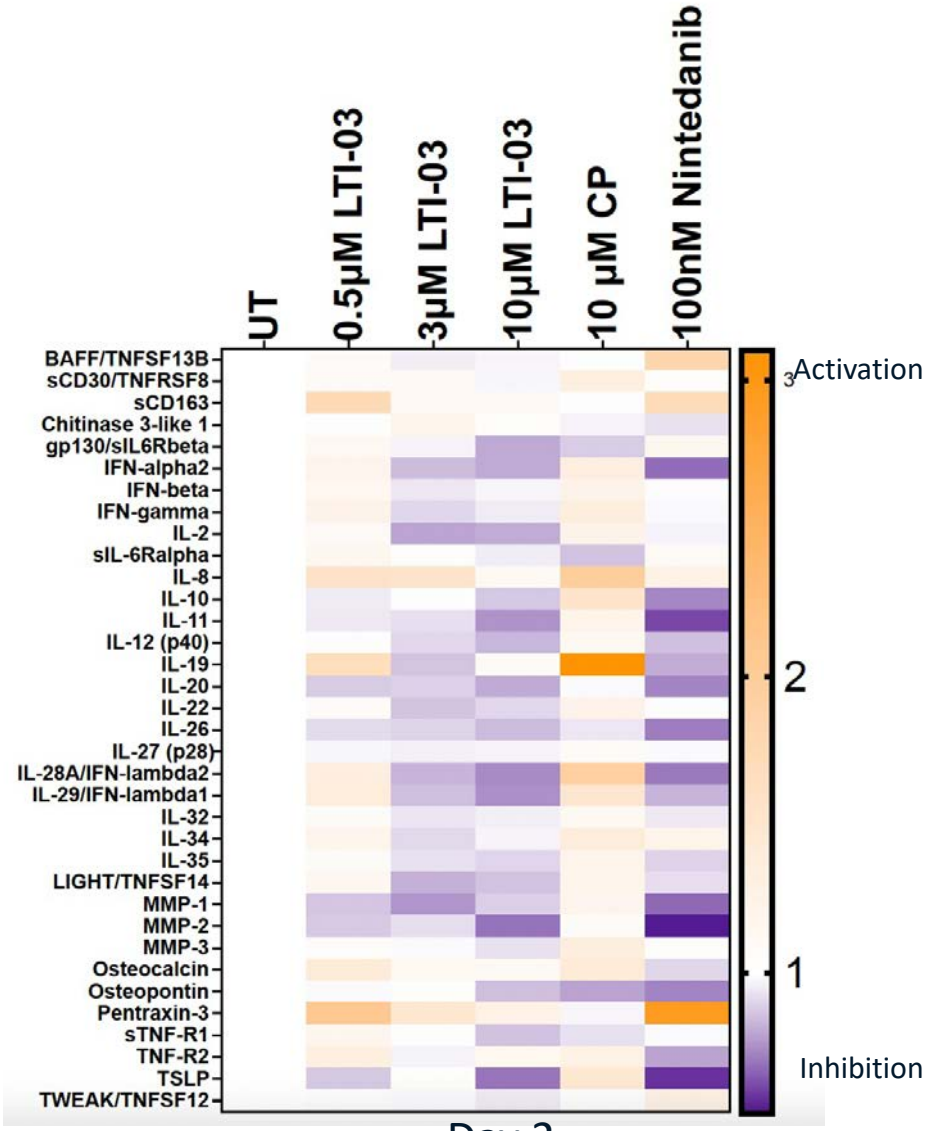


Day 2

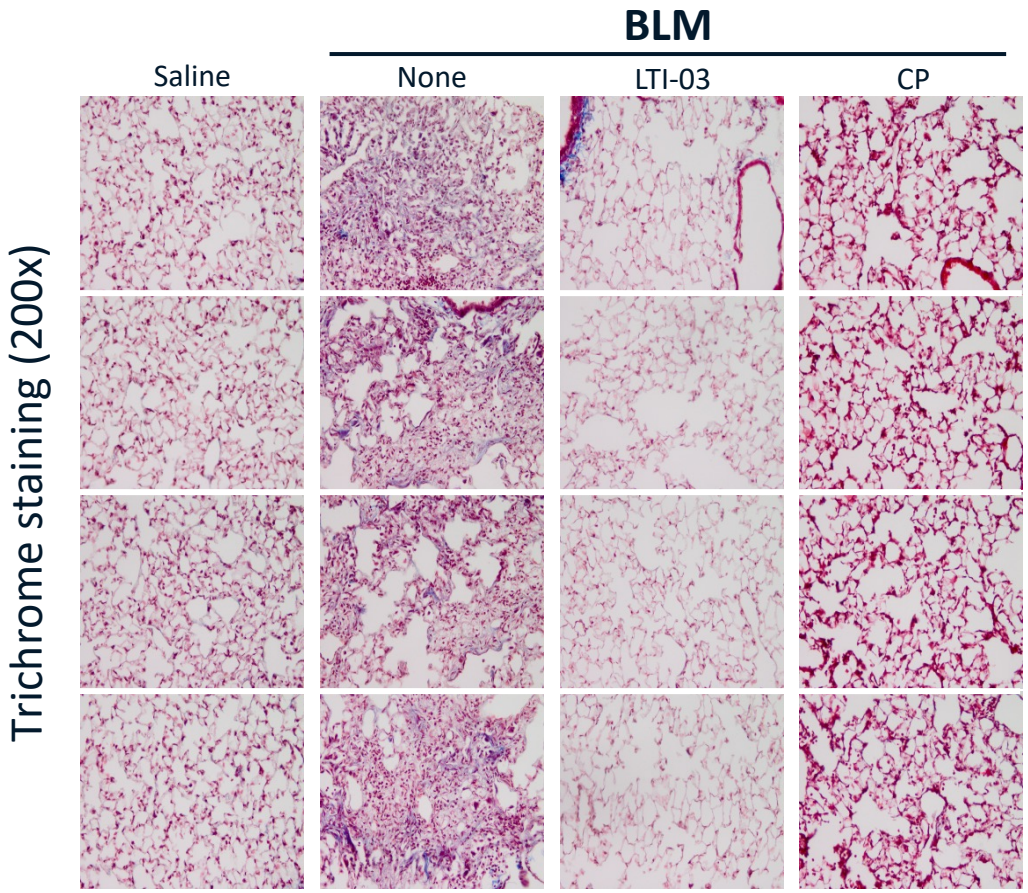


Day 4

Anti-Fibrotic Activity at Physiologically Relevant Dose (Every 12hrs in PCLS — Composite of Six Patient Samples)

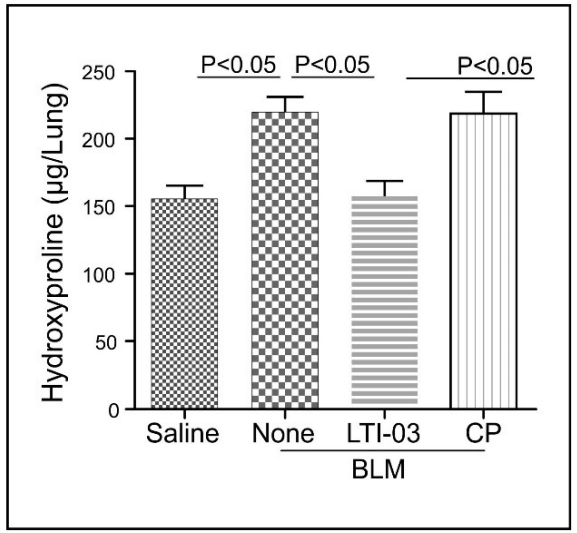


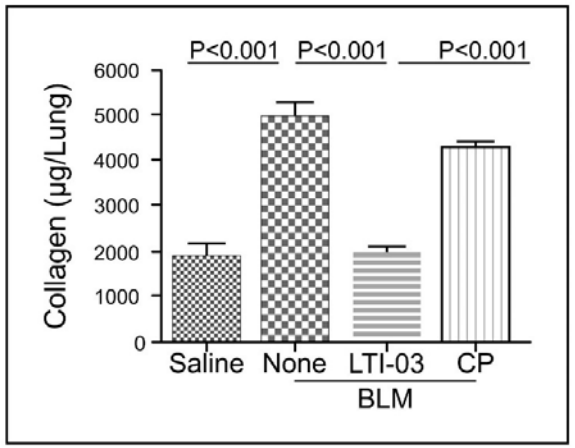
Demonstrated Anti-Fibrotic Properties in the 21-day Bleomycin Mouse Model of IPF



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

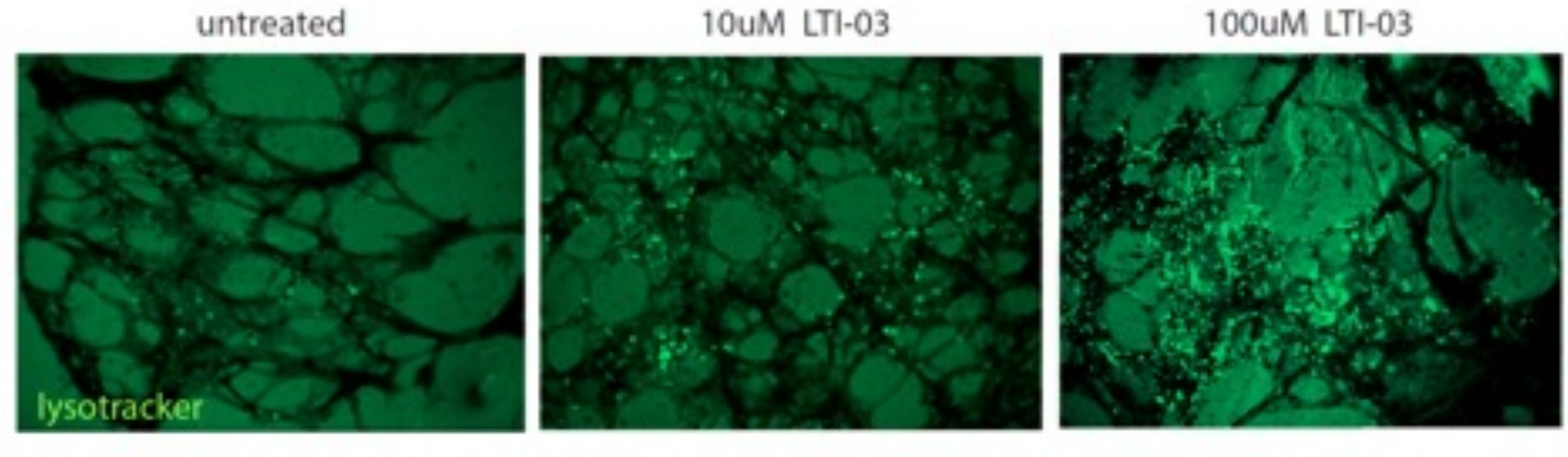
Fibrotic biomarkers





Amarnath Satheesh Marudamuthu et al. Caveolin-1–derived peptide limits development of pulmonary fibrosis.Sci. Transl. Med.11,eaat2848(2019).DOI:10.1126/scitranslmed.aat2848

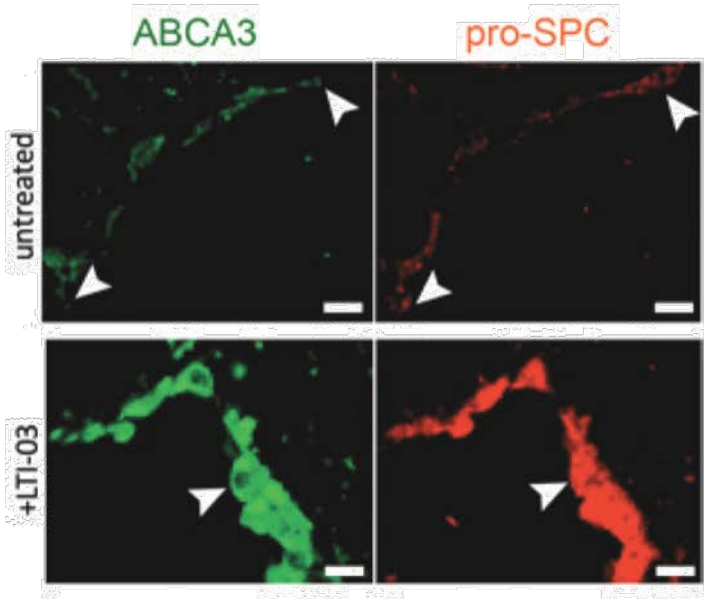
Dose Dependent Increase in Lysotracker Staining in Fibrotic PCLS Model (48hrs following single treatment)



LTI-03 Supports IPF Tissue Epithelium (Fibrotic PCLS Model)

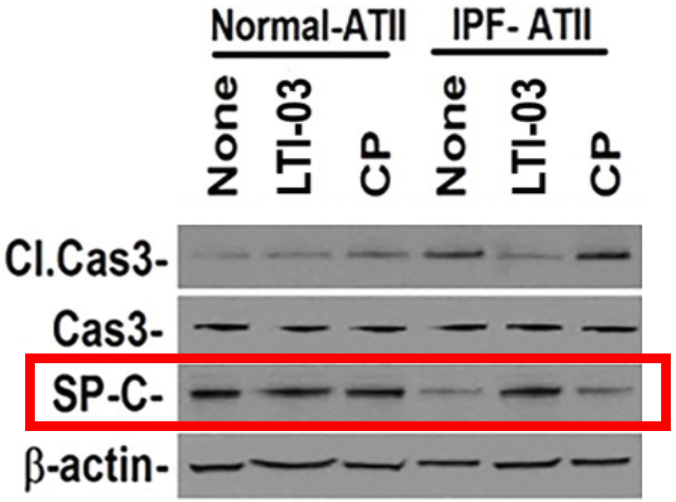
Immunofluorescent Staining for AEC2 Markers

Increases in lysotracker staining also correlated with increases in pro-SPC and ABCA3 gene (the pro-SPC transporter)



SPC is essential for lung function

LTI-03 also increases levels of SP-C in PCLS IPF Tissue

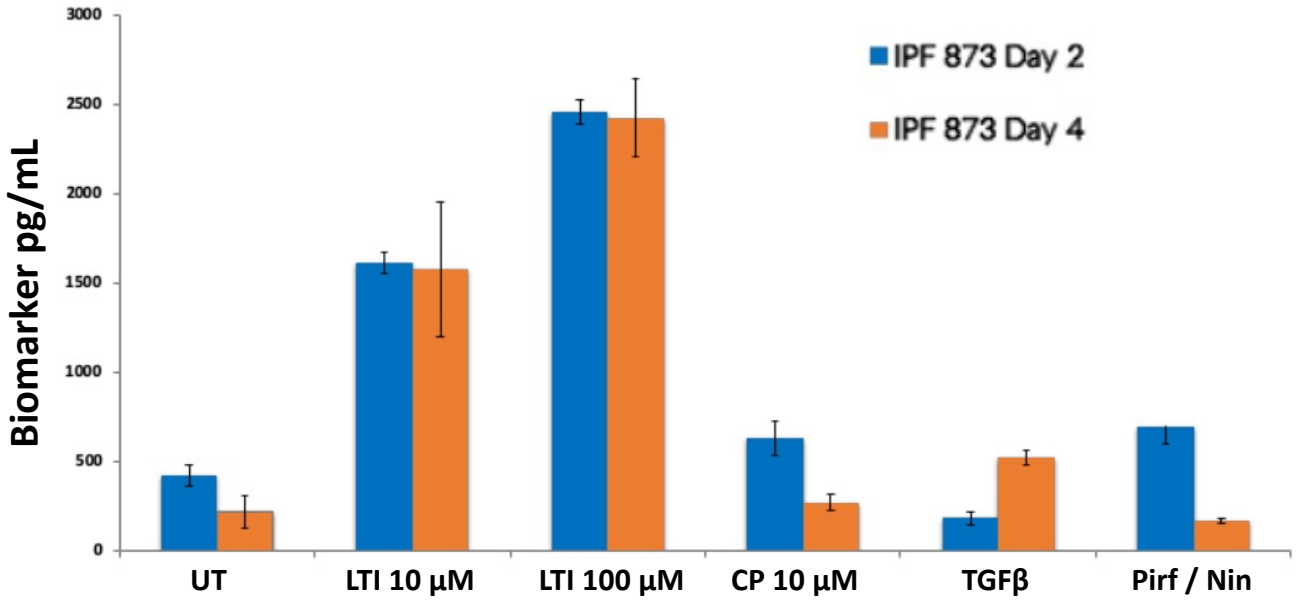


- In addition to producing AEC1s that make up the majority of the alveolar surface and are **important for proper gas exchange** and ion/water flux, AEC2s **also produce surfactant** that provides for **adequate lung expansion**

Novel Prognostic Biomarker Data Supports LTI-03 Protection of Epithelial Cells

Biomarker Correlates with LTI-03 Impact in PCLS System

Administration of LTI-03 in the PCLS system increased the soluble protein biomarker, sRAGE, while currently approved therapies had negligible effects on sRAGE levels



***Low levels** of sRAGE at diagnosis predict poor survival in IPF*[1]

The increase in sRAGE** provides further evidence of increased AEC2 survival, leading to **greater AEC1 production** and thus **overall epithelial cell survival

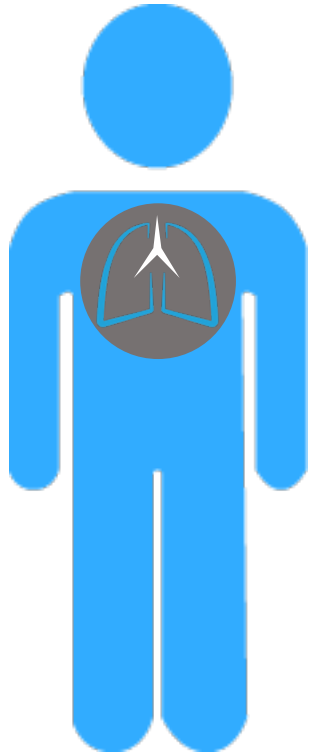
*Ability to **measure sRAGE in broncho-alveolar lavage fluid and blood** makes it a potentially **useful biomarker***

[1]Machahua, C., Montes-Worboys, A., Planas-Cerezales, L. et al. Serum AGE/RAGEs as potential biomarker in idiopathic pulmonary fibrosis. Respir Res 19, 215 (2018).

Phase 1a Clinical Trial Design (Status: Complete)

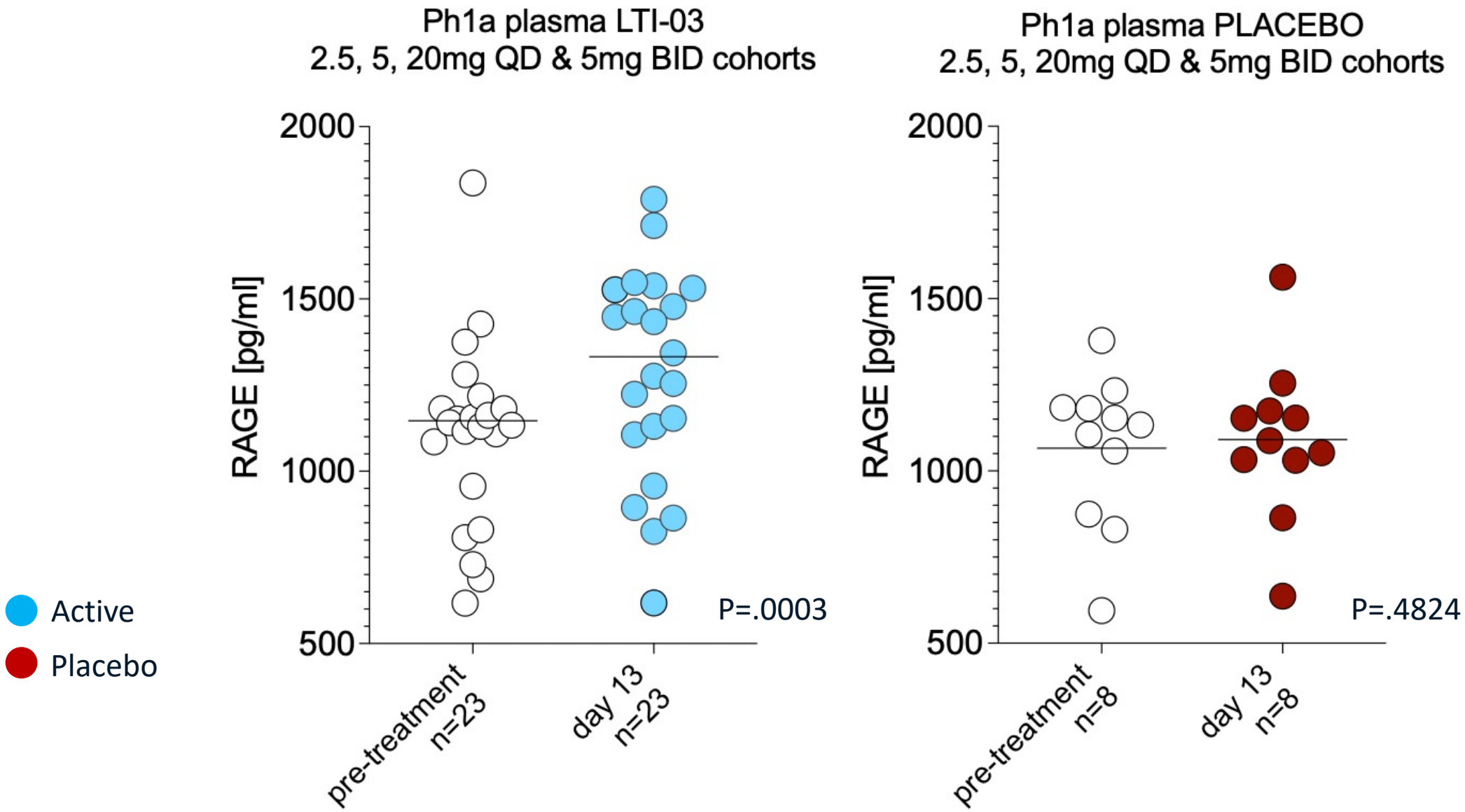
Healthy Human Volunteer Clinical Trial

- 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

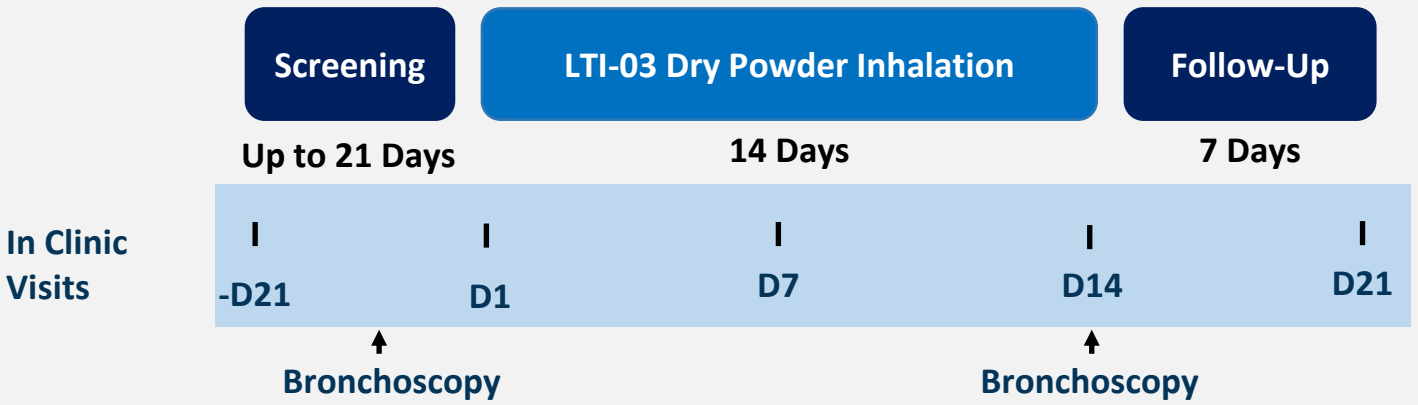


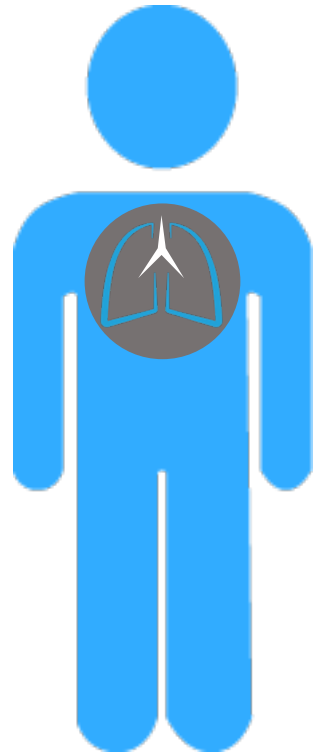
Pooled Dose Groups (2.5-20 mg) – Stat Sig Increase in sRAGE from Day 0 to Day 13 Treatment

Post-hoc analysis



Phase 1b Clinical Trial Design (Status: In Process)





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 endpoint: Biomarkers (blood, BAL, brushings)

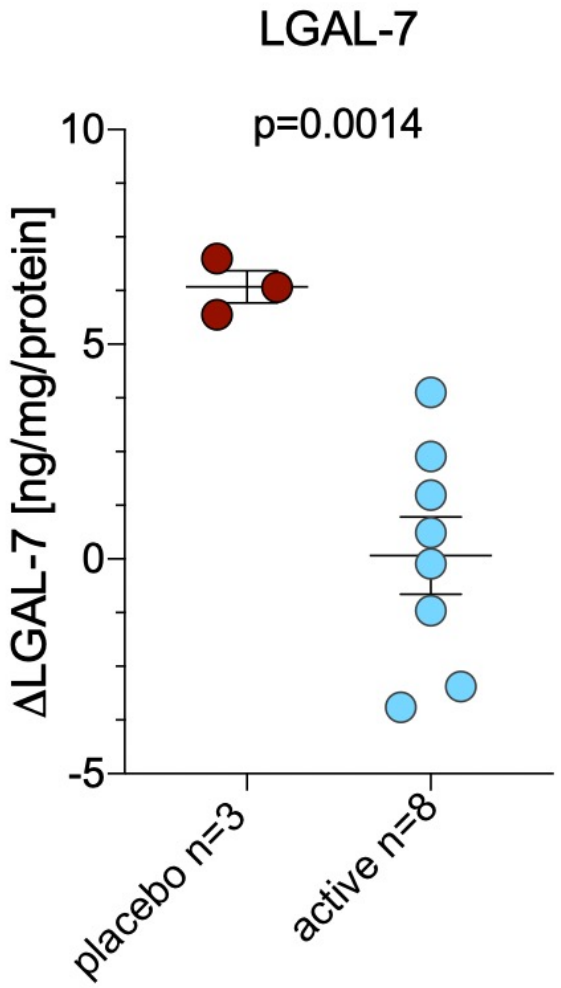
Phase 1b Clinical Trial
Cohort 1 (low dose)

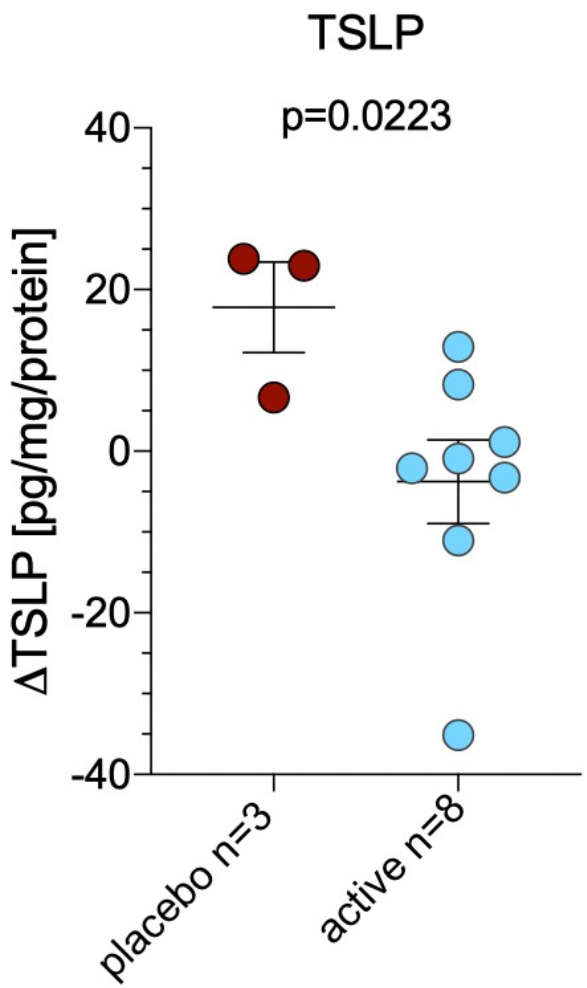
Biomarkers	Positive Trend	Statistically Significant
Fibroblasts/myofibroblasts		
Col-1α1	✓	✓
IL-11	✓	
CXCL7	✓	
p-SMAD2/3; total SMAD2/3		
Basal-like cells		
TSLP	✓	✓
GAL-7	✓	✓
Alveolar epithelial health		
sRAGE	✓	
Inflammation/safety		
p-AKT/total AKT	✓	

Placebo n=3 Active n=8

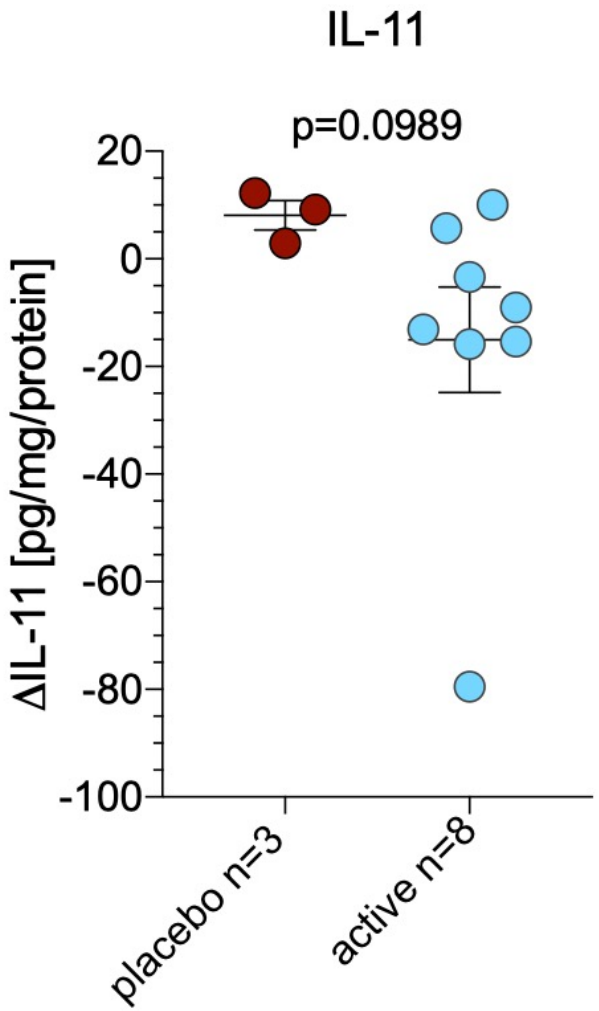
- ***Low dose LTI-03:***
- reduced expression of **multiple profibrotic proteins** in both **pathologic basal-like cells** and **fibroblasts**
- Stimulated production of a factor indicative of **type I epithelial cell health**.
- **did not induce inflammation in PBMCs**

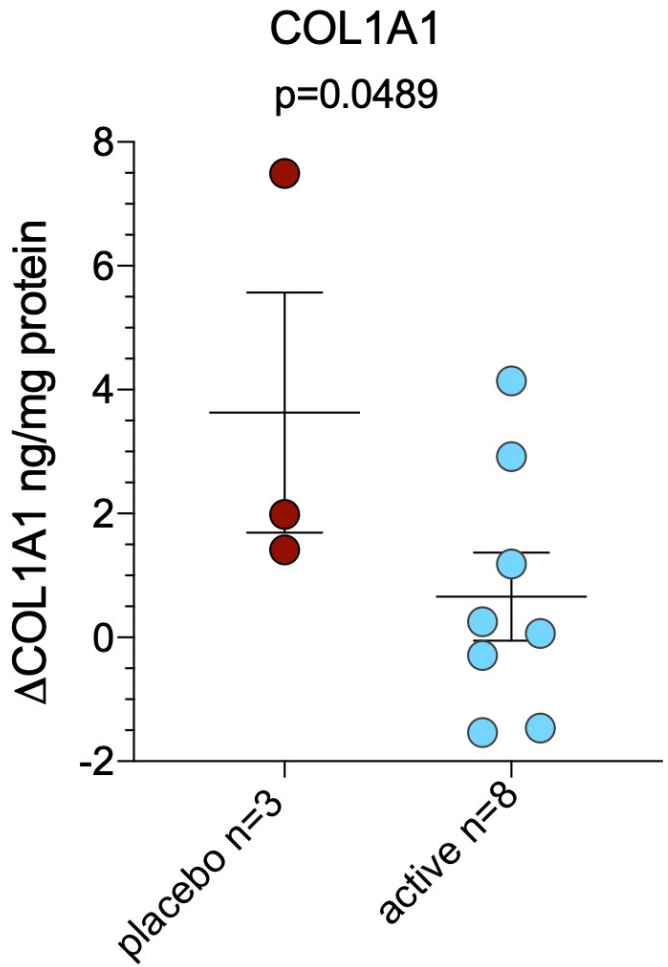
LTI-03 Phase 1b Biomarker Support Data – Gal-7 and TSLP



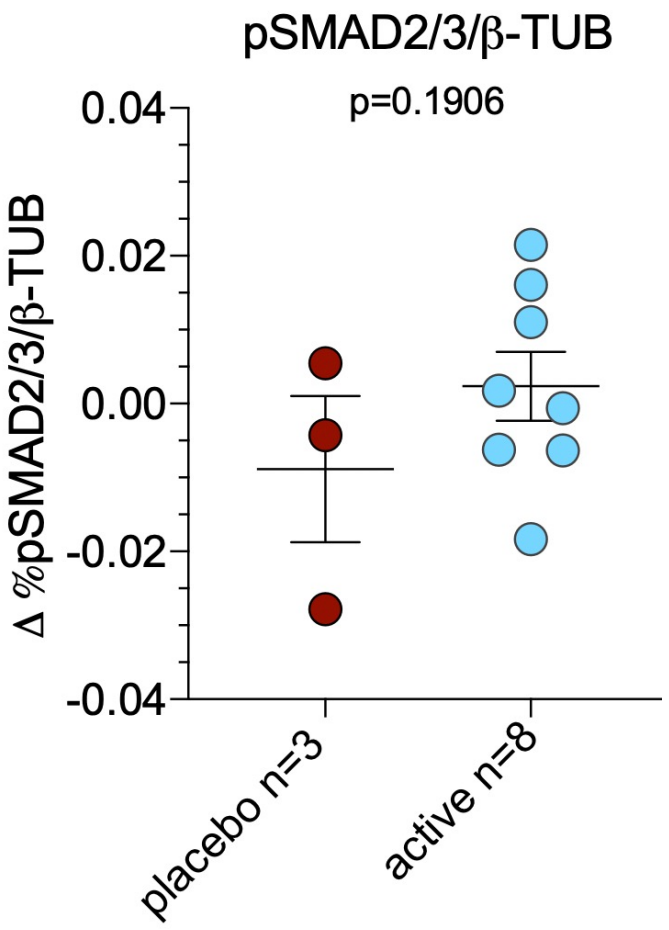


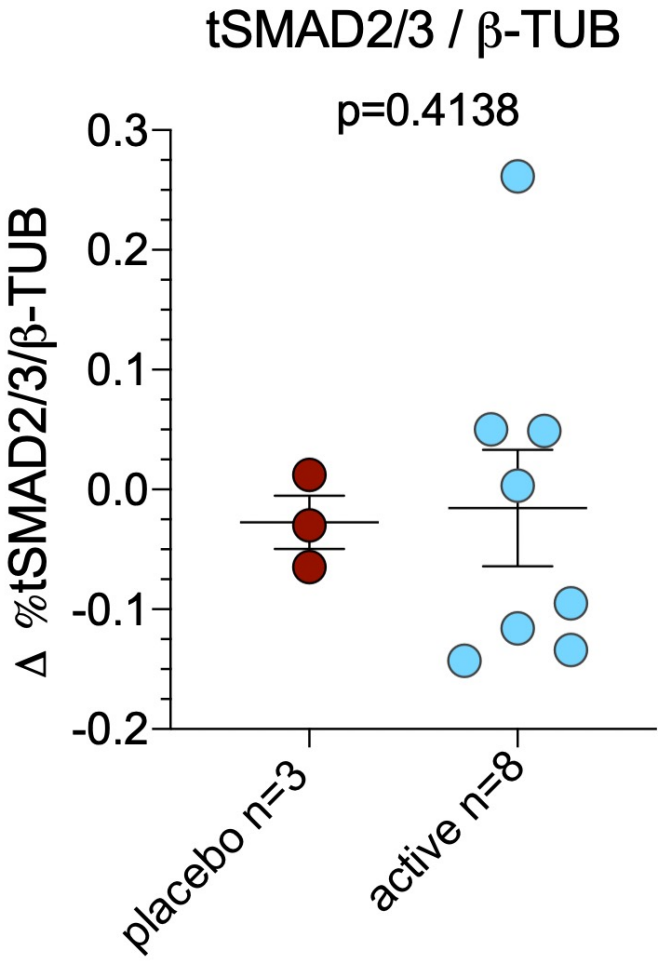
LTI-03 Phase 1b Biomarker Support Data – IL-11 and COL1A1



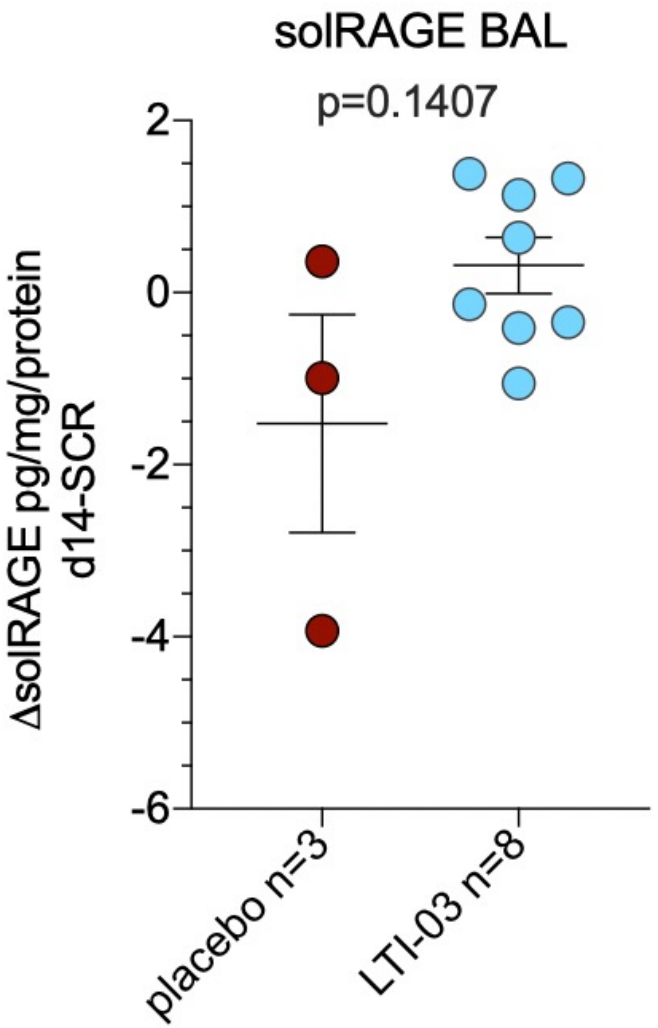


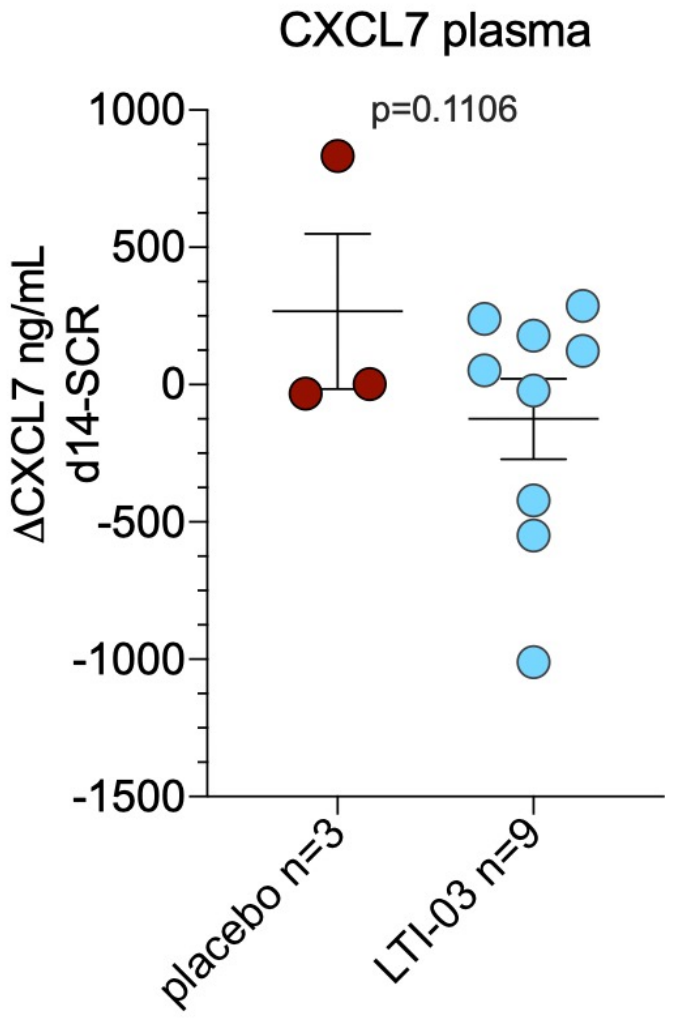
LTI-03 Phase 1b Biomarker Support Data – pSMAD 2/3 and tSMAD 2/3



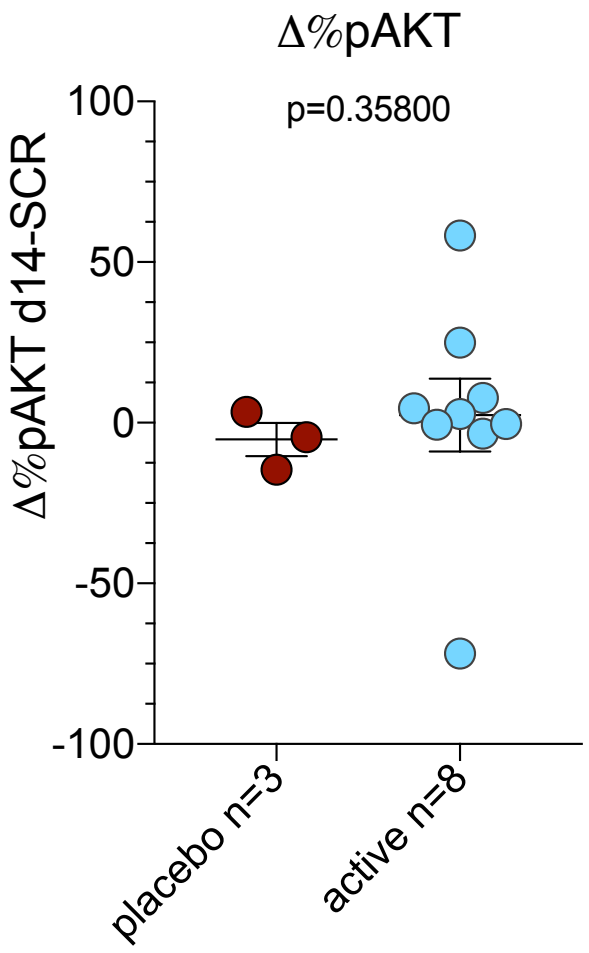


LTI-03 Phase 1b Biomarker Support Data – solRAGE and CXCL7

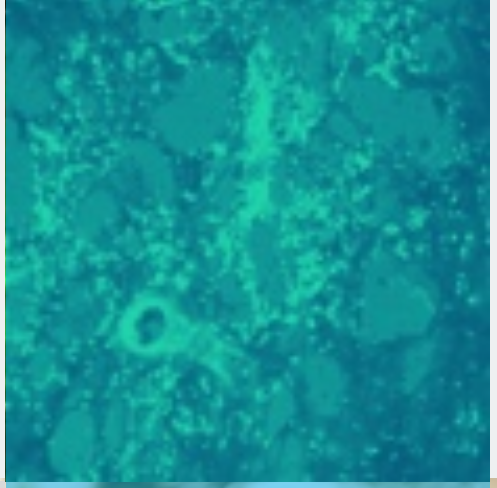


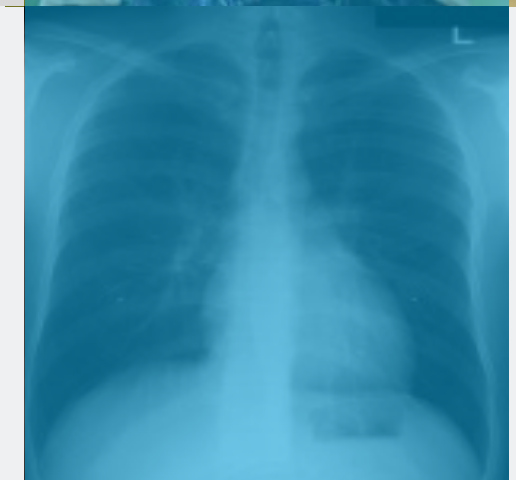


LTI-03 Phase 1b Biomarker Support Data - pAKT



LTI-01: Enzyme Therapy for Loculated Pleural Effusions





LTI-01 is a PAI-1 Resistant Plasmin Activated Proenzyme in Development for Loculated Pleural Effusions

- Hospital indication – significant population from pneumonia patients with an estimated population of over 60,000[1] patients in the US alone annually
- Current treatment options are surgery and/or off label fibrinolytic use
  - Surgery is expensive and invasive with longer hospital stays
  - Fibrinolytic use is used off label and has safety concerns
- Based on animal model studies and mechanism, LTI-01 has potential to provide longer duration of activity, eliminate repeated daily dosing and confer a lower risk of bleeding[2]
- Physician market studies support the use of fibrinolytics and need for on-label treatment alternative to surgery
- Partnership with Taiho Pharma for development and commercialization rights in Japan

1 Management estimate

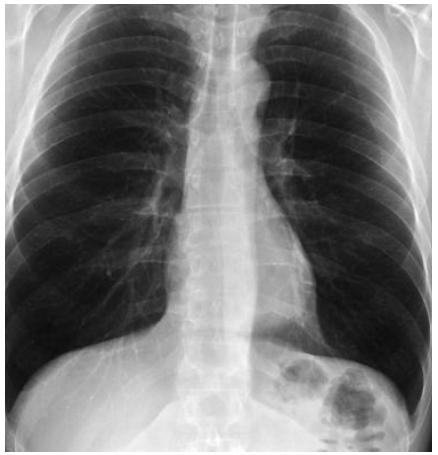
2 Komissarov et al. Novel aspects of urokinase function in the injured lung: role of α2-macroglobulin. Am J Physiol Lung Cell Mol Physiol. 2012 Dec 15;303(12):L1037-45. doi: 10.1152/ajplung.00117.2012. Epub 2012 Oct 12. PMID: 23064953; PMCID: PMC3532585.

There Are No Approved Drug Treatments for Loculated Pleural Effusion

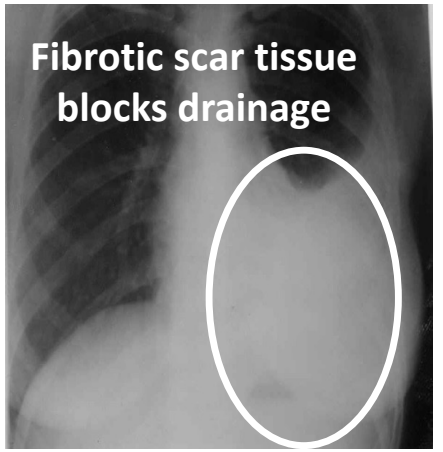
Disease Overview

- 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[1]
- LPE is managed with tPA/DNase (off-label) and/or surgery (costly and invasive)

Healthy Lungs



Loculated Pleural Effusion

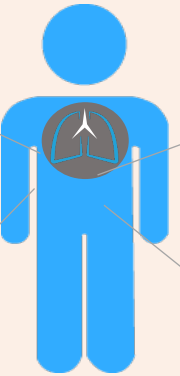


Current treatment options for patients with LPE are limited

Surgery

91% Effective[2]

- Long hospital recovery (20-25 days)
- Risk of pain and complications
- Increased morbidity
- **Invasive and expensive**



Off-Label Fibrinolytics

56% Effective[3]

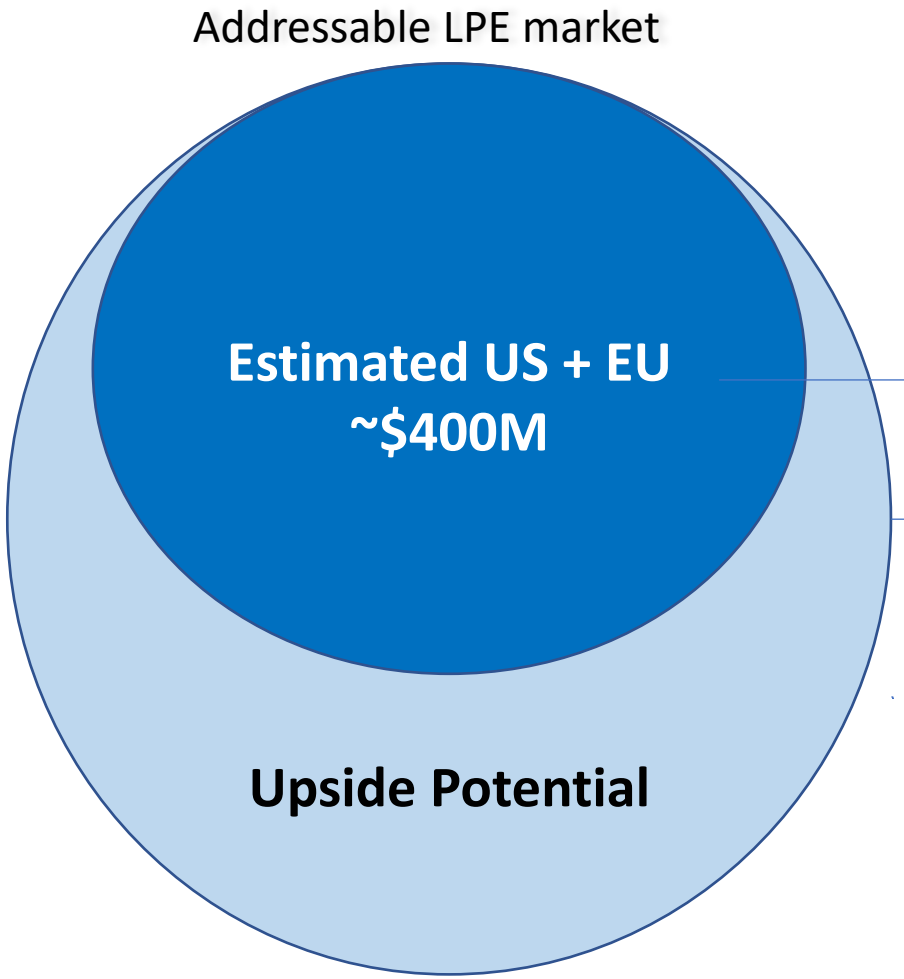
- Less costly and risky than surgery
- Many patients still need surgery
- **Not FDA approved**

[1] KarandashovaS, Florova G, Idell S, Komissarov AA. From Bedside to the Bench-A Call for Novel Approaches to Prognostic Evaluation and Treatment of Empyema. Front Pharmacol. 2022 Jan 20;12:806393. doi: 10.3389/fphar.2021.

[2] Wait MA, Sharma S, Hohn J *et al.* A randomized trial of empyema therapy. *Chest* 1997; **111**: 1548– 51.

[3] Retrolysis Study raw data, Jason Akulian

Sizeable US and EU Commercial Opportunity with Potential Upside



Current US and EU LPE 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 alternative

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

+ Japan partnership with TAIHO PHARMA

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

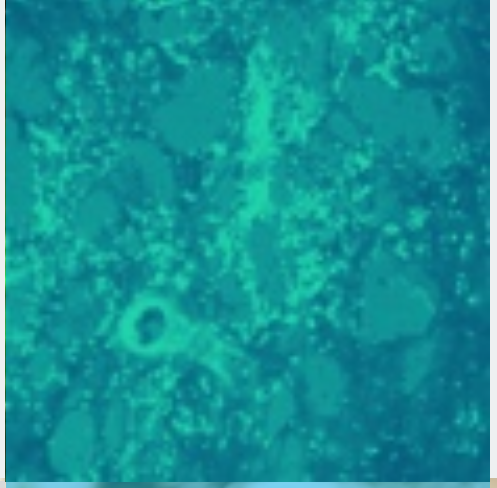
Evaluated in Phase 2a Randomized, Placebo Controlled Clinical Trial

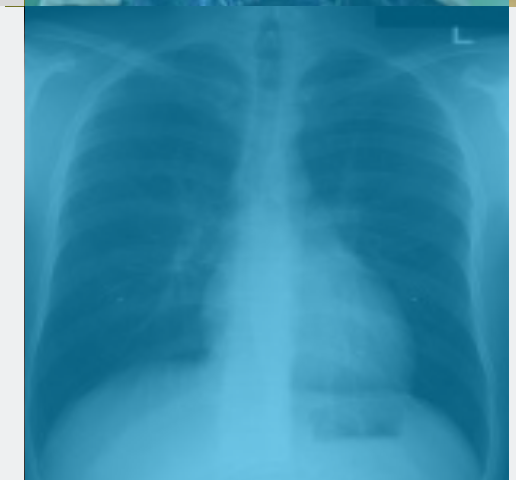
- Enrollment limited by Covid pandemic (treating physicians are interventional pulmonologists in hospital setting)

Treatment Success	LTI-01 (400,000 U) N=10	LTI-01 (800,000 U) N=9	LTI-01 (1,200,000 U) N=10	All LTI-01 N=29	Placebo N=11
Primary end pt - Per Protocol, n (%)	7 (77.7%)	6 (66.6%)	5 (55.5%)	18 (66.6%)	7 (63.6%)
Primary end pt - mITT, n (%)	7 (70%)	6 (66.6%)	5 (50%)	18 (62.1%)	7 (63.6%)
No Rescue Therapy – mITT, n (%)	**6 (60%)**	**5 (55.5%)**	**4 (40%)**	**15 (51.7%)**	**3 (27.3%)**
Odds Ratio (OR)	0.26	0.31	0.49	0.33	
P value (vs Placebo)	0.147	0.221	0.463	0.161	

The Modified Intent-to-Treat (ITT) population consists of all subjects who are randomized in the study, received any doses of study medication and have at least one post baseline efficacy assessment
Difference in primary end point and no rescue therapy is patients that did not meet criteria of treatment failure checklist but were deemed to need rescue by physician.

IP Summary





Strong IP Position for All Programs and Orphan Drug Designation for Both Clinical Assets

LTI-01

- Issued method of use US patent (7,332,469)[1]
- Orphan Drug Designation in US and EU[2]
- May be eligible for a first to file BLA market exclusivity of 12 years

LTI-03

- 5 issued US patents (compositions and methods of use)
- 10 pending US patent apps
- 21 pending foreign patent apps
- Orphan Drug Designation in US[3]

FDA | ORPHAN PRODUCTS DEVELOPMENT | EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH | EMA ORPHAN DRUG DESIGNATIONS

1 Under exclusive license
2 Orphan Drug Designation in the US and EU for the treatment of empyema.
3 Orphan Drug Designation in the US for the treatment of IPF.

NASDAQ: ALRN

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