# *A New Approach to Interstitial Lung Disease*

March 2025

# Forward Looking Statements

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This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the uses for which they are being studied. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involved a number of assumptions and limitations, and you are cautioned not to give undue weight to such 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.

# Corporate Highlights

- **Major Phase 3 catalyst for multi-billion dollar indication in Q325**

- **Strong cash position with runway through key upcoming readouts and subsequent potential BLA submission for efzofitimod in pulmonary sarcoidosis**

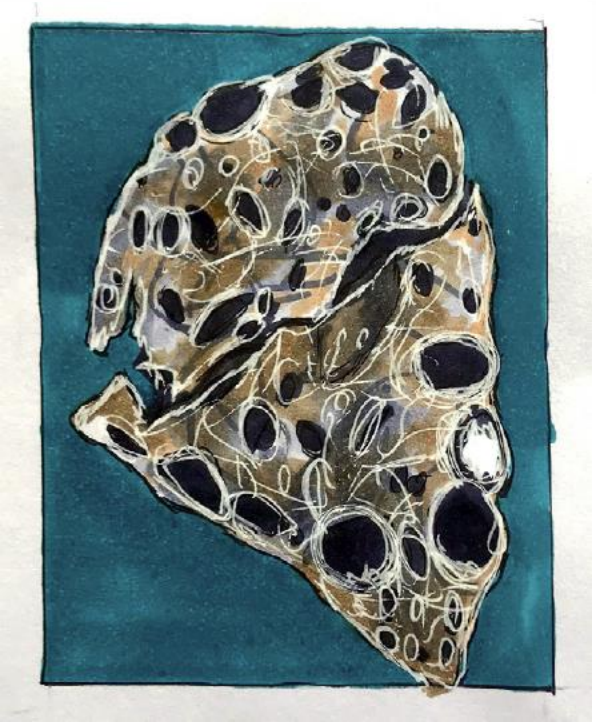
- **Pipeline targeting inflammation and fibrosis built on novel tRNA synthetase biology platform**



BLA = Biologics License Application

# A New Approach to Interstitial Lung Disease (ILD)

- ILD are a group of **severe inflammatory and fibrotic lung diseases**
- Persistent inflammation leads to **worsening lung function, fibrosis** and **poor quality of life (QoL)**
- Progressive fibrosis can result in a **survival rate that is worse than many common cancers**
- Current therapeutic options are **toxic** and **not disease modifying**



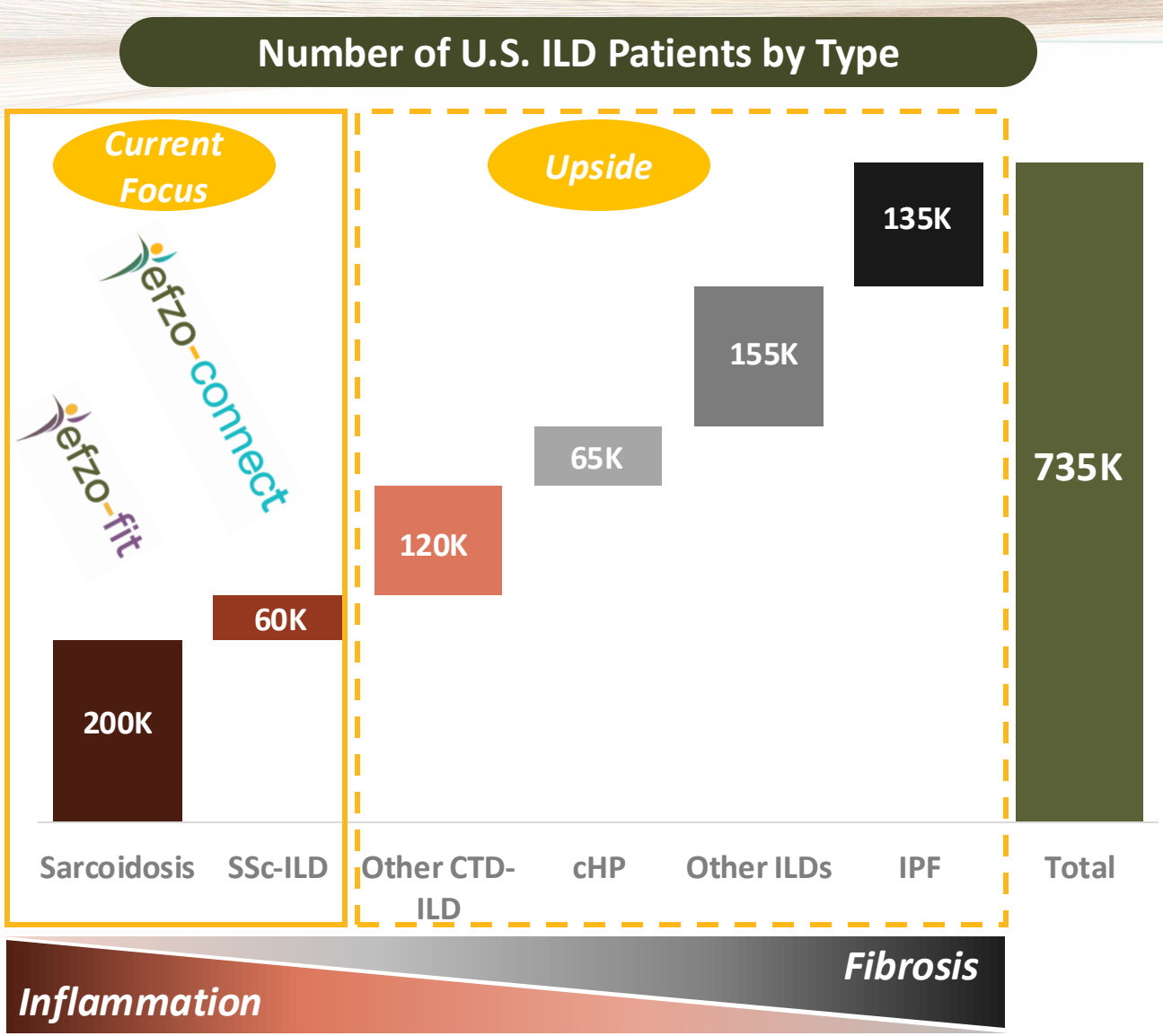
End stage fibrotic lung*

**Efzofitimod is a first-in-class biologic immunomodulator with a novel mechanism of action in Phase 3 development to address the significant unmet medical need in ILD**



*Schimmel et al. The Endless Frontier of tRNA Synthetases. *The Enzymes.* 2020

# aTyr is Advancing Efzofitimod as the Standard-of-Care for ILD

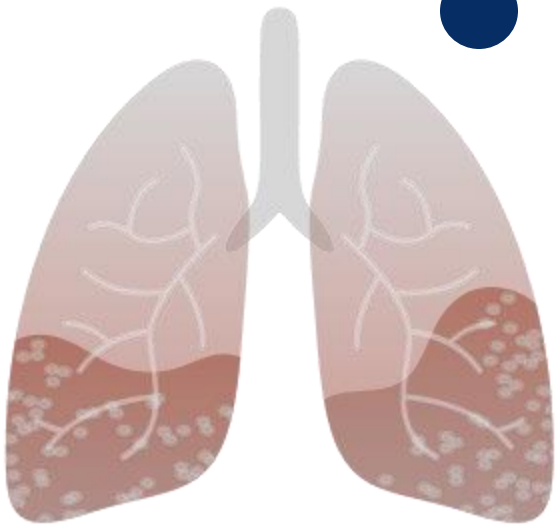



- ILD is an umbrella term for >200 types of rare lung diseases that span a spectrum of inflammation and fibrosis
- Patients have poor quality of life with high morbidity and mortality
- No disease-modifying therapies available; current options have significant toxicities
- aTyr's current focus estimated at $2-5b global market opportunity(1)
- Upside potential in other ILD and related autoimmune diseases (e.g., SSc, lupus, RA)



(1) Based on aTyr internal estimates, Back Bay Life Science Advisors market research and 2024 third party claims data analysis

# Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

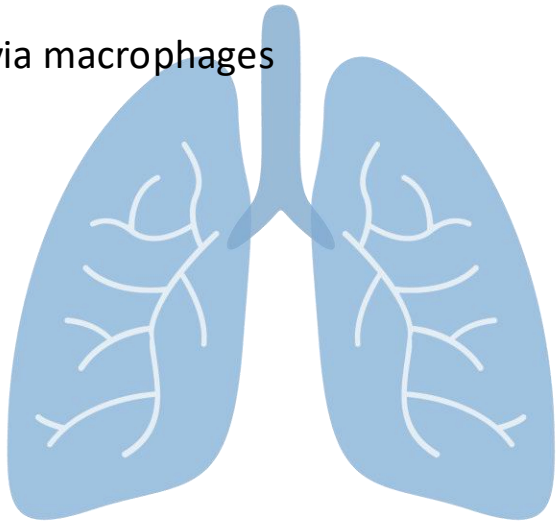


**Targets innate immunity at site of inflammation**

- downregulates pro-inflammatory and pro-fibrotic pathways via macrophages
- addresses complex immune pathology
- restores immune balance without evidence of suppression

**Promising clinical proof-of-concept**

- Reduced OCS
- Improved lung function
- Resolved symptoms



**No known significant safety issues**



OCS = oral corticosteroids

# Pulmonary Sarcoidosis

## A Major Form of Interstitial Lung Disease with High Unmet Medical Need

# Sarcoidosis is an Orphan Lung Disease with High Unmet Medical Need

## Disease Pathology

- Inflammatory disease of unknown cause
- Characterized by granulomas, or clumps of immune cells
- Can affect almost any organ; 90% of cases affect the lungs

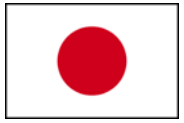
## Diagnosis

1) Compatible clinical presentation
2) Non-necrotizing granulomatous inflammation
3) Exclusion of alternative causes

## Epidemiology

200,000 pts

150,000 pts



20,000 pts

*>1 million pts worldwide*

age of onset between **30-50**

twice as common in women

**3x**

as common in African Americans

## Prognosis

**70%**

of patients need treatment within first 3 years

**20%**

of patients will develop lung fibrosis

- 1/12 patients hospitalized for their disease annually
- Mortality rising: 1/5 Medicare patients die every 3 years – 60% higher risk than general population
- Fibrosis and concomitant pulmonary hypertension biggest predictors of mortality



U.S. epidemiology and prognosis confirmed by 2024 third party claims data analysis

# Sarcoidosis Patients Suffer from Both High Disease & Treatment Burden

**Sarcoidosis robs patients of their QoL**

Nonlinear journey to diagnosis; patients plagued by shortness of breath, persistent dry cough and severe fatigue

**Major socioeconomic impact**

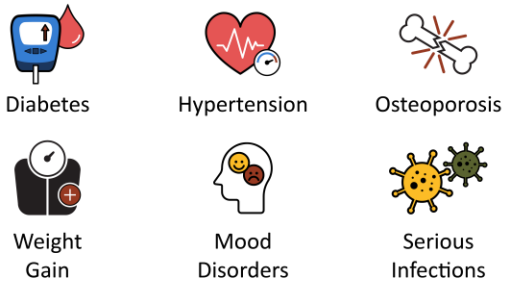
Loss of ability to work, potentially disabling

**1/5 patients will progress to fibrosis**

Higher risks of pulmonary hypertension, organ failure & death


**Corticosteroids remain first line SoC**

Short term benefit, but continued use results in debilitating side effects; getting patients off OCS becomes primary goal

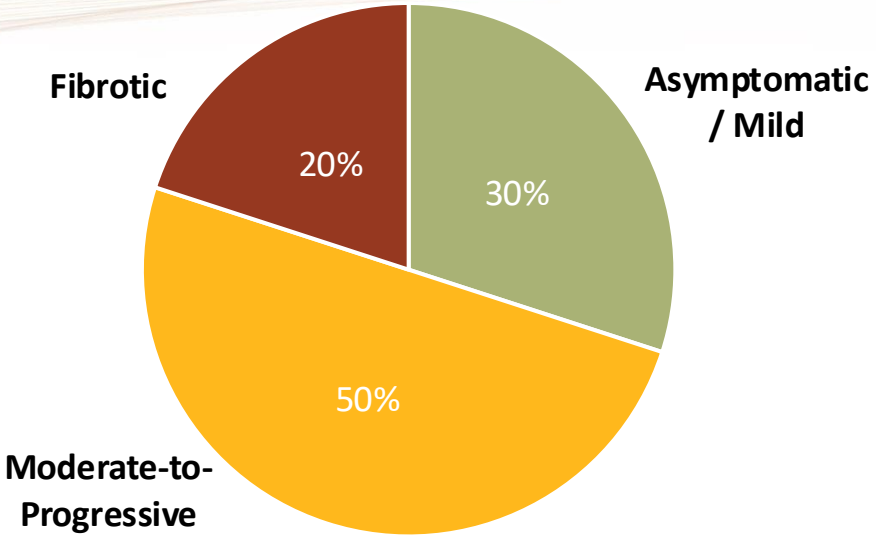



**Limited alternatives available**

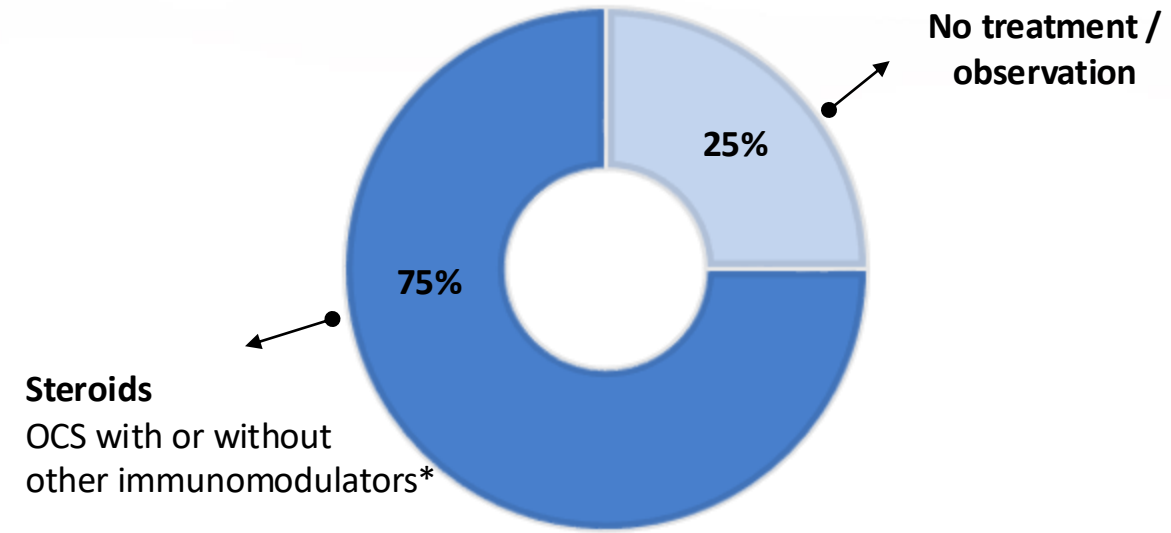
Off-label rheumatology drugs are physicians' only options, with limited evidence in sarcoidosis

# Efzofitimod Target Population for Sarcoidosis

## Disease Severity




## Current Treatment




### Efzofitimod Positioning

- Front line as a steroid-sparing agent in moderate-to-severe patients
- Reduce / eliminate steroids and avoid use of cytotoxic immunosuppressants and anti-TNFs
- Addressable population: **50-75% of all sarcoidosis patients**(1)



(1) Based on 2024 third party claims data analysis

OCS = oral corticosteroids; *minimal antifibrotic use

# Multiple Benchmarks Support Premium Pricing for New Rare Disease Treatments

$200K*

TAVNEOS (avacopan)

Livdelzi seladelpar

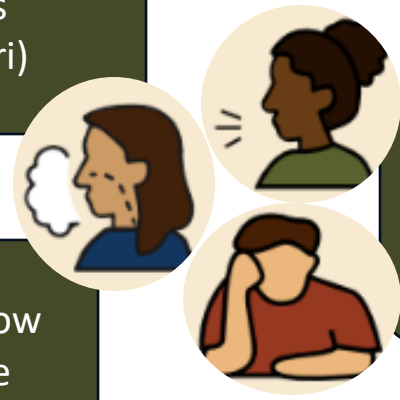
Nucala (mepolizumab)

OFEV nintedanib

FILSPARI

ACTEMRA tocilizumab

Steroid-sparing agents for inflammatory disorders (Tavneos, Nucala, Filspari)



Rare disease drug launches in recent years (Tavneos, Livdelzi, Filspari)

ILD treatments that slow lung function decline (Ofev, Actemra)

**Efzofitimod is positioned to be the first approved product for sarcoidosis in >60 years with limited competition**

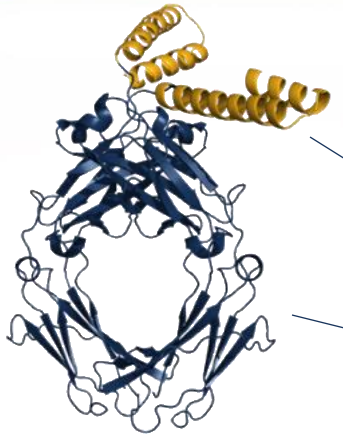
*Estimated annual cost of comparative products based on list price and labeled dosing in the U.S.

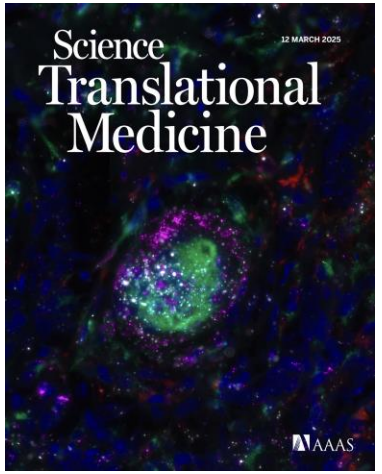
# Efzofitimod

## First-in-Class Biologic Immunomodulator for Interstitial Lung Disease

# Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

- Innovative engineering for lung enriched HARS creates novel Fc fusion protein with enhanced PK activity
- Selective binding to NRP2 on macrophages is upstream of other targets in ILD
- Anti-inflammatory and anti-fibrotic effects demonstrated in multiple ILD models support clinical development in ILD
- NRP2 expression in sarcoid granulomas and systemic sclerosis skin Macrophages provide strong scientific rationale for initial ILD indications
- Desirable safety profile demonstrated to date
- Clinical proof-of-concept demonstrated in pulmonary sarcoidosis



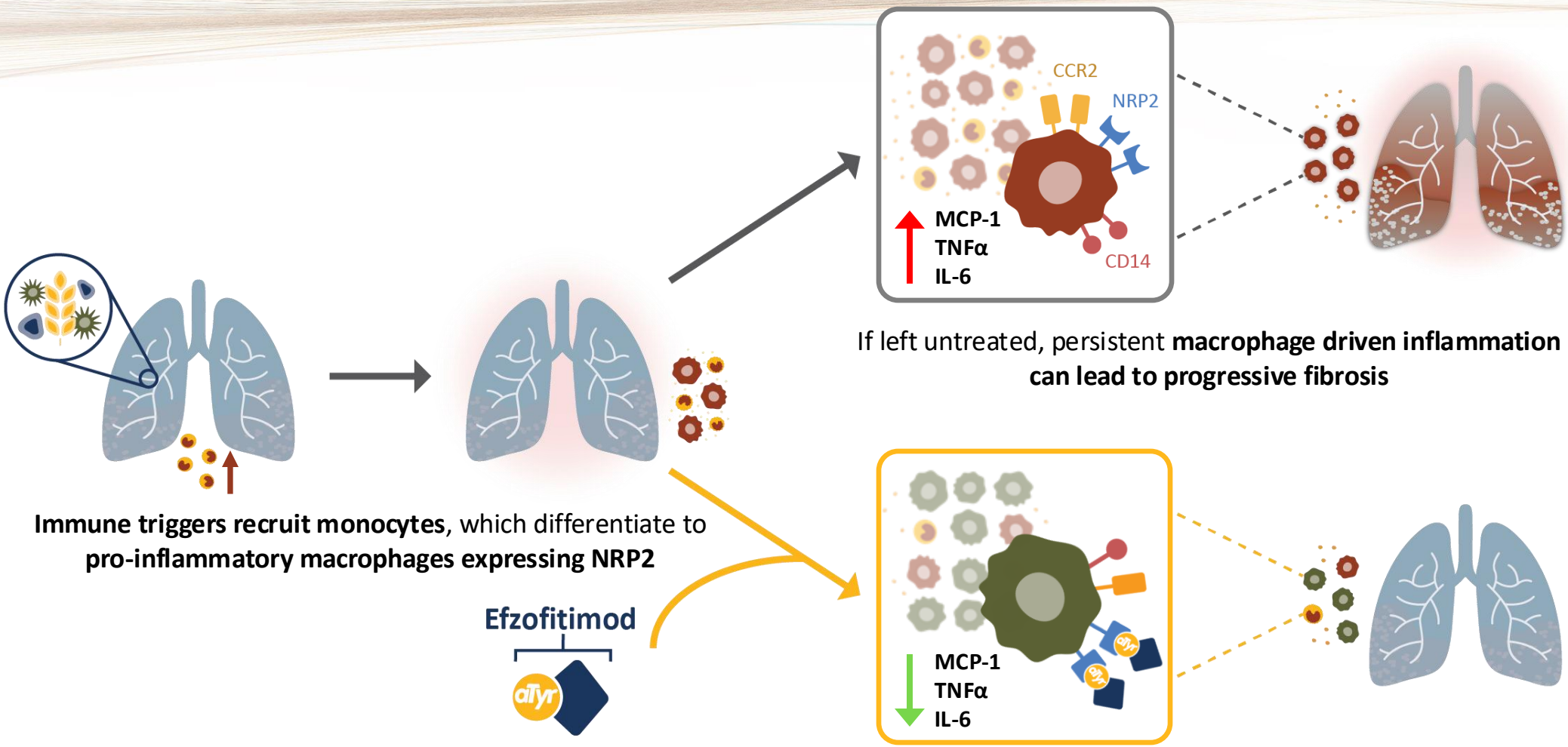




**Predicted U.S. commercial exclusivity into 2039 based on composition of matter patents, with expected patent term extension and regulatory exclusivity programs**



HARS = histidyl-tRNA synthetase; NRP2 = neuropilin-2

# Efzofitimod Modulates Macrophages to Reduce Key Drivers of Inflammation & Fibrosis




If left untreated, persistent **macrophage driven inflammation can lead to progressive fibrosis**

**Immune triggers recruit monocytes**, which differentiate to **pro-inflammatory macrophages expressing NRP2**

Efzofitimod acts as an **NRP2 agonist**

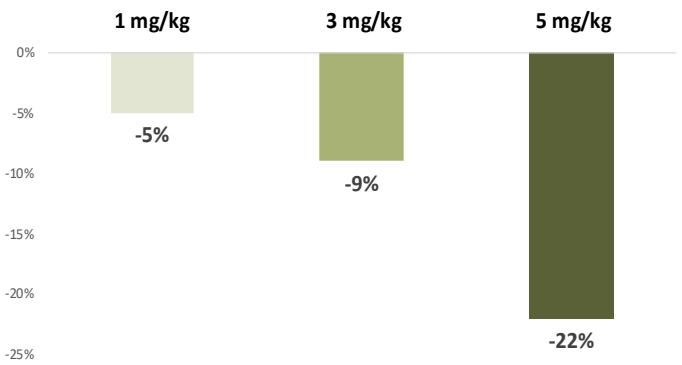
Efzofitimod promotes a less inflammatory macrophage population by **downregulating key drivers of inflammation and fibrosis**



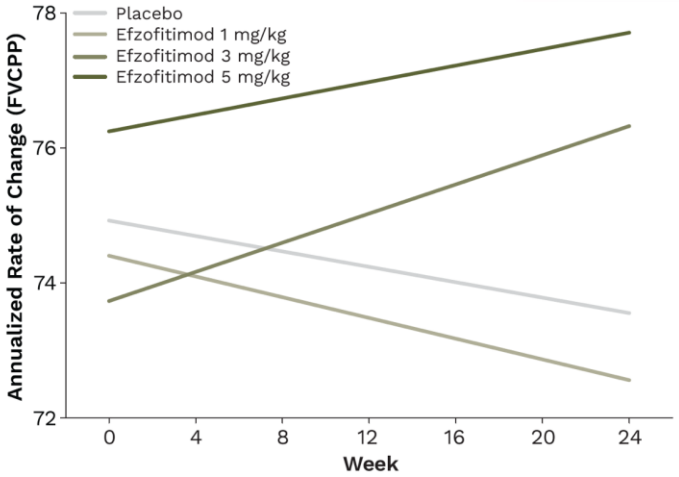
Nangle et al. *Science Translational Medicine* 2025

# Clinical Proof of Concept Demonstrated in Phase 1b/2a Pulmonary Sarcoidosis Trial

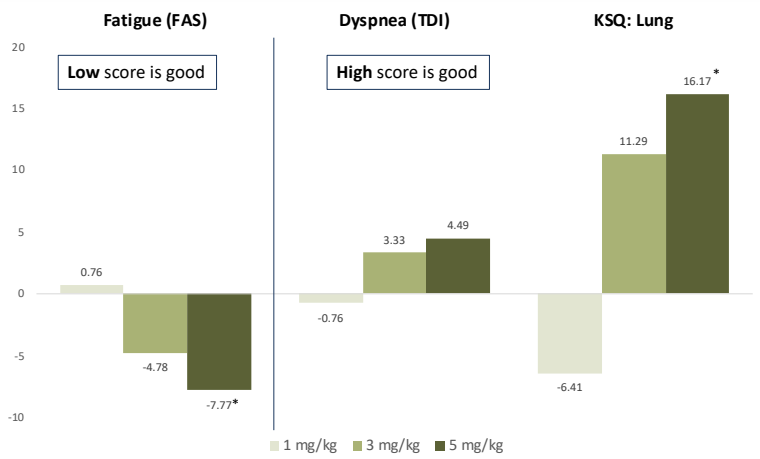
## Reduction in Avg Daily OCS vs Placebo*




## Lung Function




## Symptom Improvement vs Placebo




- Primary objective met: Efzofitimod was **safe and well-tolerated** (n=37)
- Secondary objectives met: **Dose-response observed** across all three families of pre-specified endpoints compared to placebo
- Dose-dependent **reduction of inflammatory biomarkers**
- Improvements in **time-to-first steroid relapse** and **steroid relapse rate** for 3.0 and 5.0 mg/kg efzofitimod


CHEST JOURNAL

DIFFUSE LUNG DISEASE: ORIGINAL RESEARCH | ARTICLES IN PRESS

Efzofitimod for the Treatment of Pulmonary Sarcoidosis

Daniel A. Culver, DO • Shambhu Aryal, MD • Joseph Barney, MD • ... Nelson Kinnersley, PhD • Gennyne Walker, PhD • Robert Baughman, MD • Show all authors

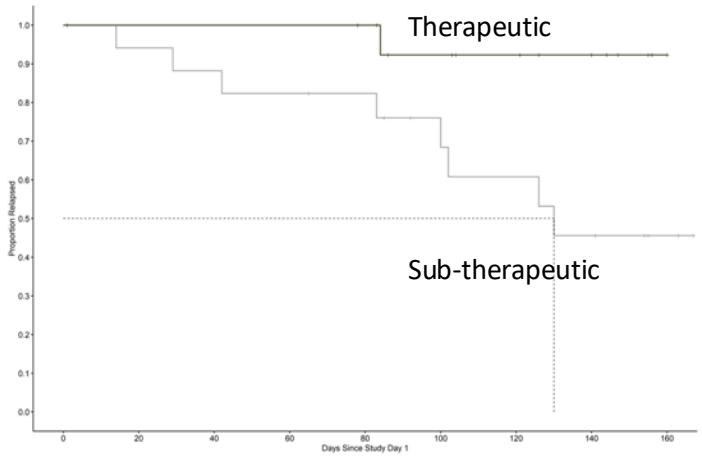


OCS = oral corticosteroids

*Post-taper

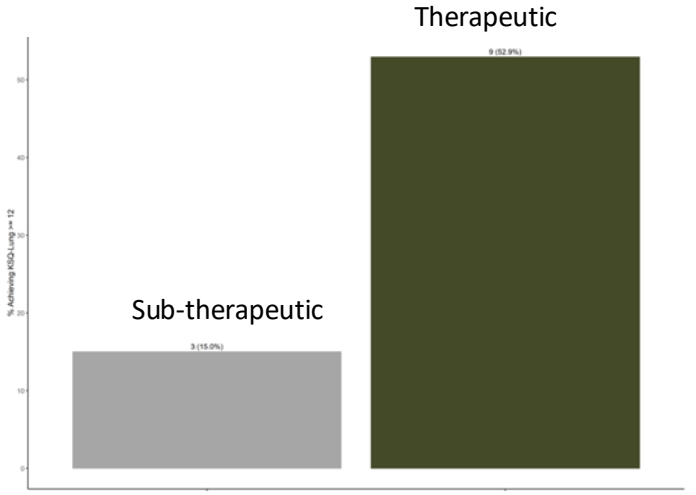
# Therapeutic Efzofitimod Doses Significantly Improve Multiple Efficacy Measures

**Time to first relapse of steroid taper**




*p = 0.017*

**% Patients with KSQ-Lung >=12**




*p = 0.032*

- Post hoc analysis from Phase 1b/2a study of efzofitimod in pulmonary sarcoidosis
- Pooled analysis comparing 3.0 and 5.0 mg/kg efzofitimod (therapeutic group) vs 1.0 mg/kg efzofitimod and placebo (sub-therapeutic group)
- Improvements in **time-to-first steroid relapse** and **steroid relapse rate** for therapeutic efzofitimod doses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**Therapeutic Doses of Efzofitimod Demonstrate Efficacy in Pulmonary Sarcoidosis**

Ogugua Ndili Obi, Robert P. Baughman, Elliott D. Crouser, Mark W. Julian, Landon W. Locke, Abhijeeth Chandrasekaran, Pavithra Ramesh, Nelson Kinnersley, Vis Niranjan, Daniel A. Culver, Peter H. S. Sporn

# Phase 3 Trial Design and Endpoints Prioritize Clinically Meaningful Outcomes for Patients

**Primary Endpoint — Steroid Reduction**

*Change from baseline in absolute OCS dose at week 48*

- Represents a clinically meaningful outcome for patients and providers
- Reflective of ERS treatment guidelines that emphasize reducing OCS

**Secondary Endpoint — KSQ-Lung**

- The most relevant patient reported outcome indicative of disease specific pulmonary symptoms

**Secondary Endpoint — FVC**

- Important measure of lung function in sarcoidosis but limited natural history data

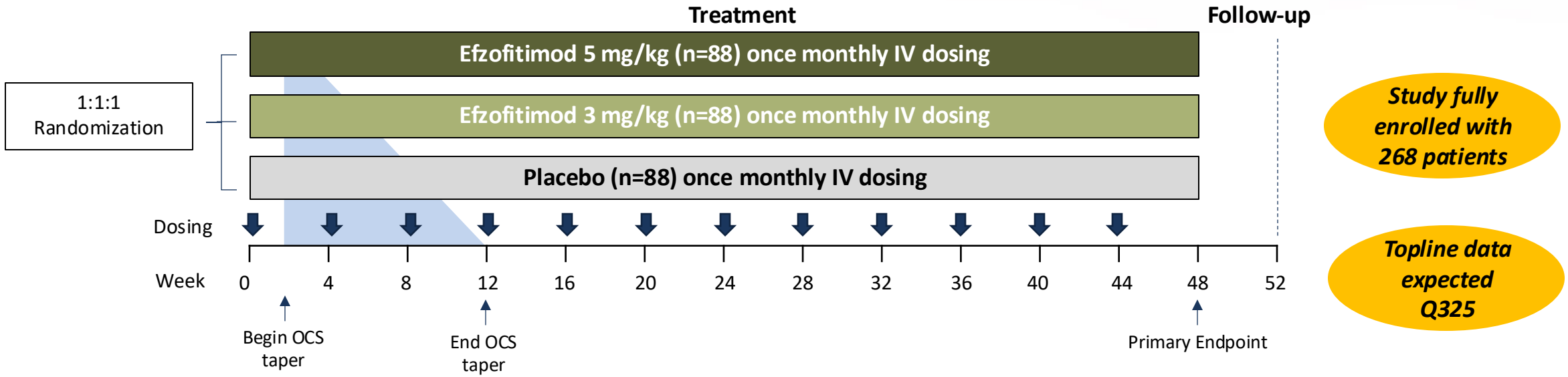
**First Phase 3 and largest interventional study conducted in sarcoidosis includes primary and secondary endpoints that represent both physiologic and quality of life measures**



FDA = Food and Drug Administration; ERS = European Respiratory Society; OCS = oral corticosteroids; FVC = forced vital capacity; KSQ-Lung = Kings Sarcoidosis Questionnaire-Lung

# Global Phase 3 Trial in Pulmonary Sarcoidosis Ongoing

**Primary objective**: Assess the efficacy of efzofitimod in patients with pulmonary sarcoidosis




**Population: moderate to severe pulmonary sarcoidosis**

- Diagnosis of pulmonary sarcoidosis for ≥ 6 months
- Stable treatment with ≥ 7.5 and ≤ 25 mg/day OCS
- Extent of fibrosis < 20%
- Symptomatic with KSQ-Lung score ≤ 70

**Steroid Taper Protocol Guidelines**

- Based on Patients Global Assessment (PGA) **and** Investigator Assessment (IA) conducted every two weeks
- If both PGA **and** IA are stable or improved, patient OCS will need to be **tapered**; If either PGA **or** IA has worsened, patient will be **rescued** with OCS

Individual Patient Expanded Access Program (EAP) is intended to allow access for patients who complete EFZO-FIT™ and wish to receive treatment with efzofitimod outside of the clinical trial

# SSc-ILD

## Indication Expansion Represents Upside Opportunity in Interstitial Lung Disease

# SSc-ILD is Common and Deadly Manifestation of Systemic Sclerosis

## Disease Pathology

- Autoimmune disease also known as scleroderma
- Characterized by inflammation and scarring, or fibrosis, of skin and other organs, including the lungs

## Diagnosis

1) ILD diagnosed secondary to underlying SSc
2) Confirmed with imaging, PFTs and blood work

## Epidemiology

*>1.5 million patients worldwide*

## Current Treatments

Mycophenolate, cyclophosphamide → Tocilizumab, rituximab → Nintedanib

- Efzofitimod positioned as 2nd line in patients who progress on or cannot tolerate MMF / CYC
- Addressable population in major markets: **>50k**(1)
- Upside potential: improve underlying systemic disease

**45-55** is the average age of onset for SSc-ILD

**3x** greater mortality risk than SSc alone

**70-90%** of ILD develops in the first three years of SSc

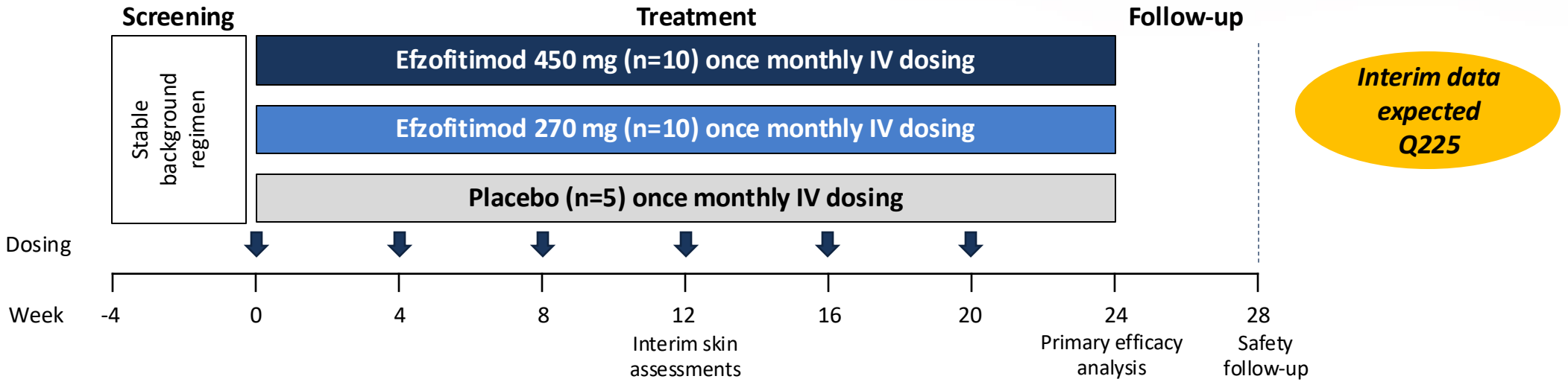
**30%** of patients develop lung fibrosis



(1) Back Bay Life Science Advisors

# Phase 2 POC Trial Enrolling in SSc-ILD

**Primary objective**: Assess the efficacy of efzofitimod on pulmonary, cutaneous, and systemic manifestations in SSc-ILD




**Population: SSc with progressive ILD**

- Patients with SSc (ACR/EULAR criteria), and ILD (baseline HRCT)
- Progressive disease (recent onset, evidence for inflammation, diffuse cutaneous SSc)
- On background mycophenolate therapy or equivalent

**Primary Endpoint**

- Lung function: forced vital capacity

**Key Secondary Endpoints**

- Symptom control: PROs
- Skin: histopathology, gene profiling, biomarkers, mRSS

Patients who complete the study are eligible to participate in a 24-week open-label extension.



POC = Proof of Concept

# A New Approach to Interstitial Lung Disease

# Efzofitimod Leads Growing Pipeline of First-in-Class tRNA Synthetase Derived Biologics

| PROGRAM | tRNA SYNTHETASE | TARGET/MOA | INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|---|---|
| **Efzofitimod** | HARS | NRP2 modulator | Pulmonary Sarcoidosis(1) | | | efzo-fit | **Topline data Q3 2025** |
| | | | SSc-ILD | | | efzo-connect | **Interim data Q2 2025** |
| | | | Other ILD (CTD-ILD; CHP) | | | Kyorin | **Japan Partner** |
| **ATYR0101** | DARS | LTBP1 modulator | Fibrosis | | | | |
| **ATYR0750** | AARS | FGFR4 modulator | Liver Disorders | | | | |
| **tRNA Synthetase Candidates(2)** | | | | | | | |

(1) In partnership with Kyorin Pharmaceutical Co., Ltd. for the development and commercialization of efzofitimod for ILD in Japan
(2) Pipeline candidates in development based on additional tRNA synthetases from IP portfolio
SSc-ILD = Scleroderma-related ILD; CTD-ILD = Connective Tissue Disease-ILD; CHP = Chronic Hypersensitivity Pneumonitis

# Corporate Summary

## Disruptive tRNA synthetase biology platform

- Extracellular tRNA synthetases represent potential new class of medicines
- IP directed to more than 200 synthetase fragments represents unique and validated drug discovery method

## Lead candidate efzofitimod for ILD represents $2-5b market opportunity

- First-in-class biologic immunomodulator with upstream target for ILD with little competition
- Topline data from Phase 3 EFZO-FIT™ study in pulmonary sarcoidosis expected in Q325 and interim data from Phase 2 EFZO-CONNECT™ study in SSc-ILD expected in Q225
- U.S. FDA orphan drug designations for sarcoidosis and SSc; Fast Track designations for pulmonary sarcoidosis and SSc-ILD; E.U. orphan drug designations for sarcoidosis and SSc; Japan orphan drug designation for sarcoidosis
- Commercial exclusivity in the U.S. anticipated into at least 2039

## Growing pipeline targeting inflammation and fibrosis

- Multiple tRNA synthetase candidates in preclinical development
- Candidates bind targets in novel ways with potential implications in high value markets

## Strong financial fundamentals

- ~$75.1m in cash, restricted cash, cash equivalents and investments as of Q424; additional $18.8m in gross proceeds raised from at-the-market (ATM) offering subsequent to Q424
- Cash runway projected for a period of one year following the Phase 3 EFZO-FIT™ readout
- Partnership with Kyorin Pharmaceutical for efzofitimod for ILD in Japan

Thank You