



*A New Approach to Interstitial Lung Disease*

J.P. Morgan Healthcare Conference

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# Forward Looking Statements

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# Corporate Highlights



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



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



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

# 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**

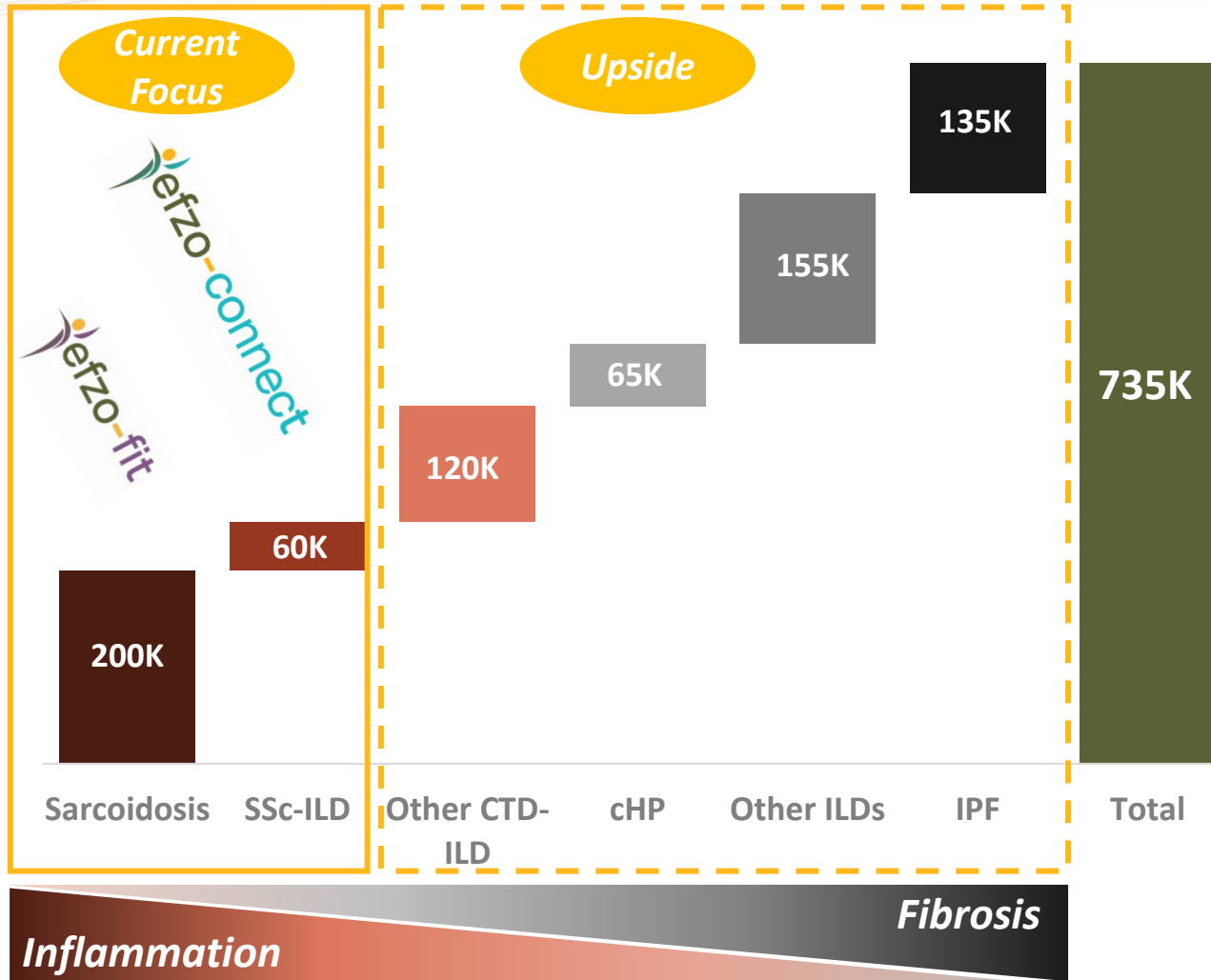


End stage fibrotic lung\*

**Efzofitimid 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**

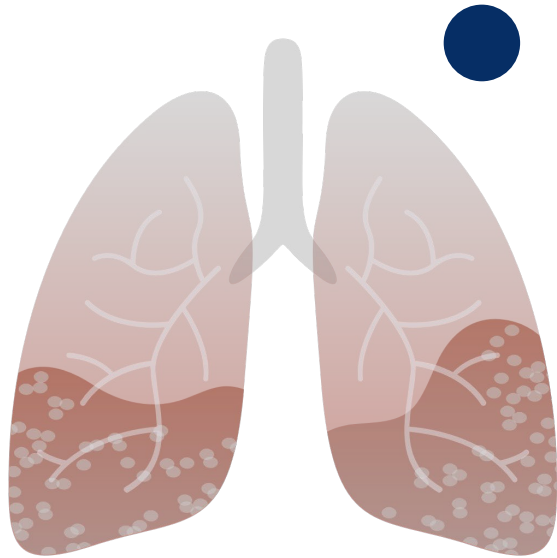
# aTyr is Advancing Efzofitimid as the Standard-of-Care for ILD

## Number of U.S. ILD Patients by Type



- 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<sup>(1)</sup>
- Upside potential in other ILD and related autoimmune diseases (e.g., SSc, lupus, RA)

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



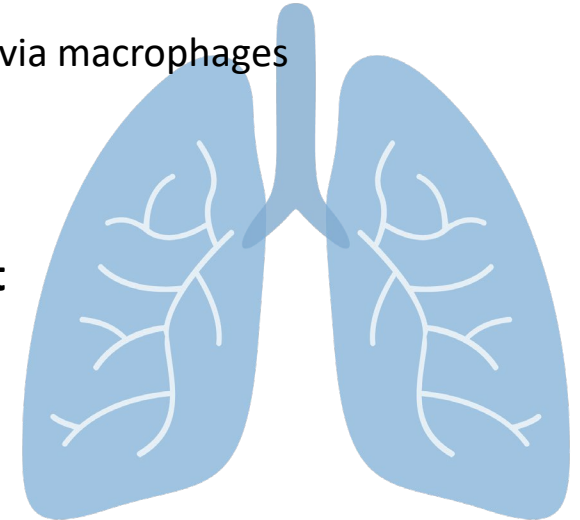
## Targets innate immunity at site of inflammation

- 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





## 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

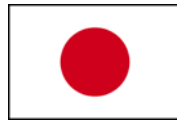
## Epidemiology



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

## Diagnosis

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

## Prognosis



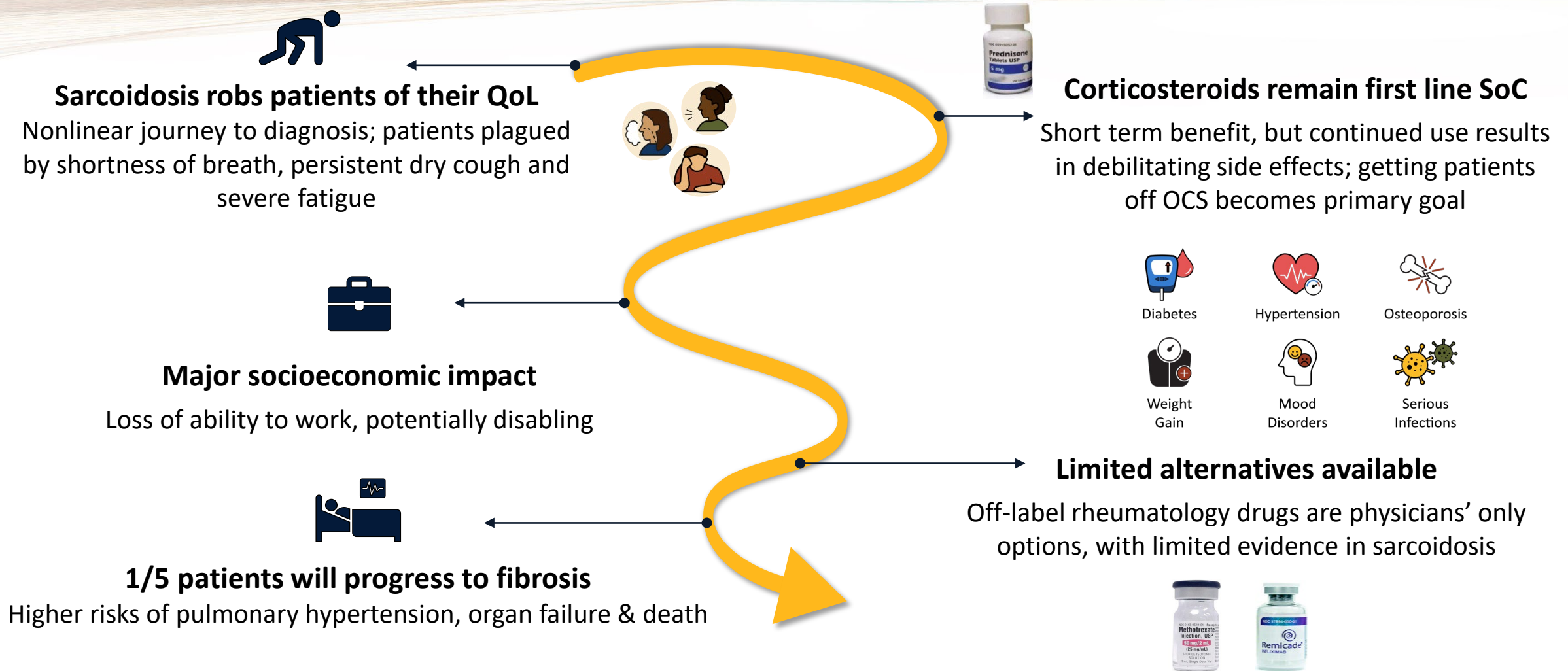
**70%**  
of patients need  
treatment within  
first 3 years



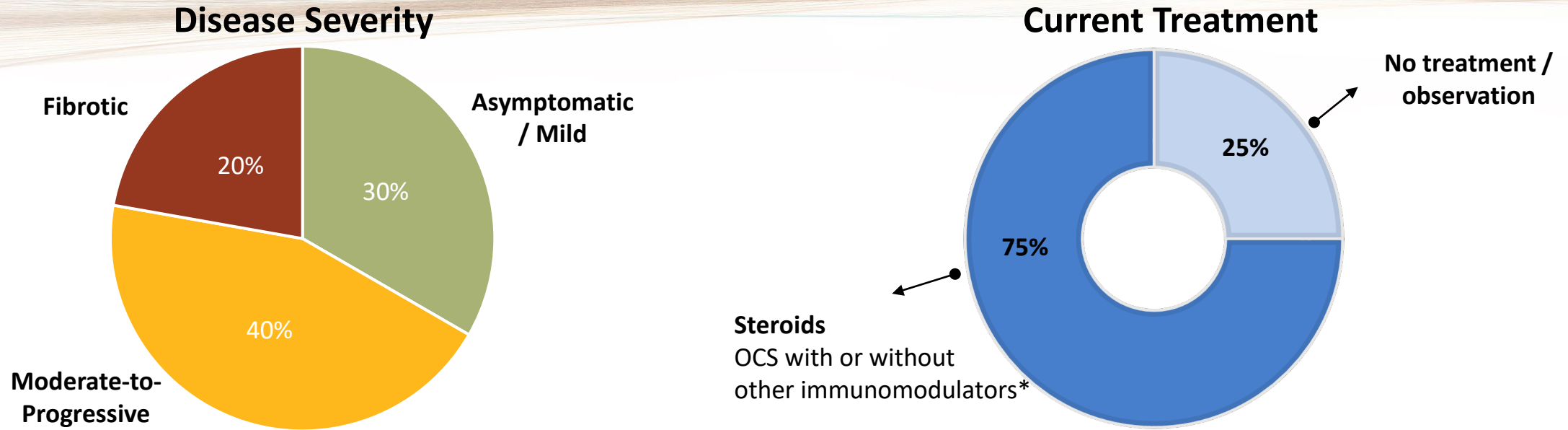
**20%**  
of patients will  
develop lung  
fibrosis

- 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 drivers of mortality

# Sarcoidosis Patients Suffer from Both High Disease & Treatment Burden



# Efzofitimod Target Population for Sarcoidosis



## 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<sup>(1)</sup>**

# 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)

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

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



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

The logo for aTyr, featuring the lowercase letters 'aTyr' in a bold, italicized sans-serif font. The 'a' is yellow, 'T' is dark green, and 'yr' is a lighter green. The background of the slide is a light green gradient with a complex pattern of thin, overlapping lines in various shades of green and yellow, creating a sense of depth and movement.

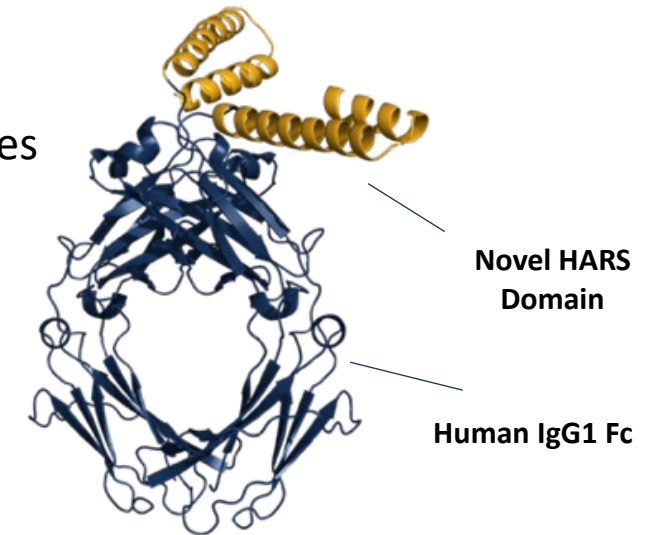
**aTyr**

Efzofitimod

First-in-Class Biologic Immunomodulator for  
Interstitial Lung Disease

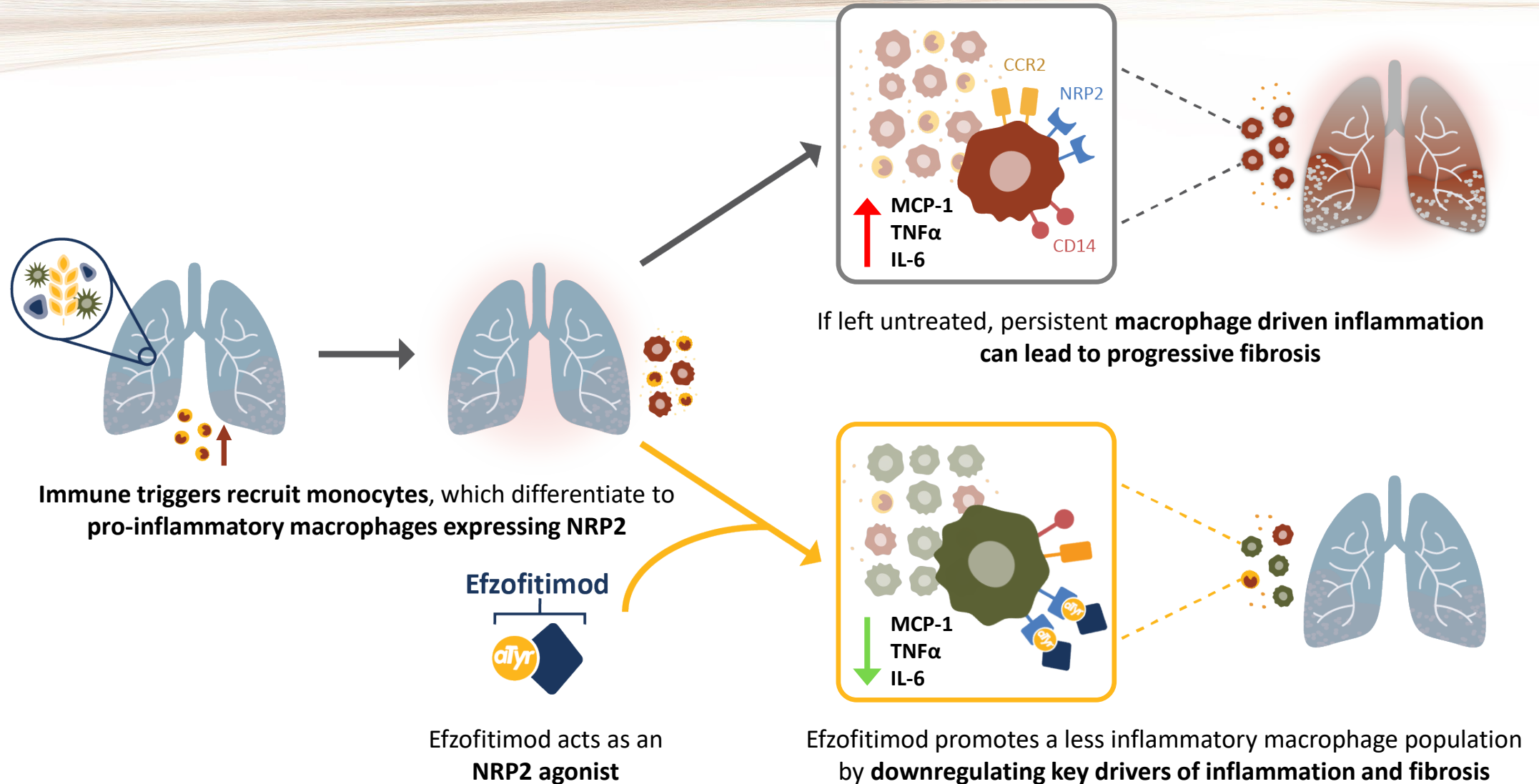
# Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

- ✓ 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



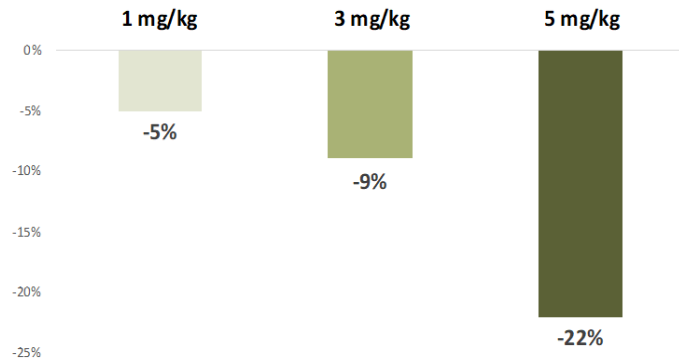
**Predicted U.S. commercial exclusivity into 2039 based on composition of matter patents, with expected patent term extension and regulatory exclusivity programs**

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

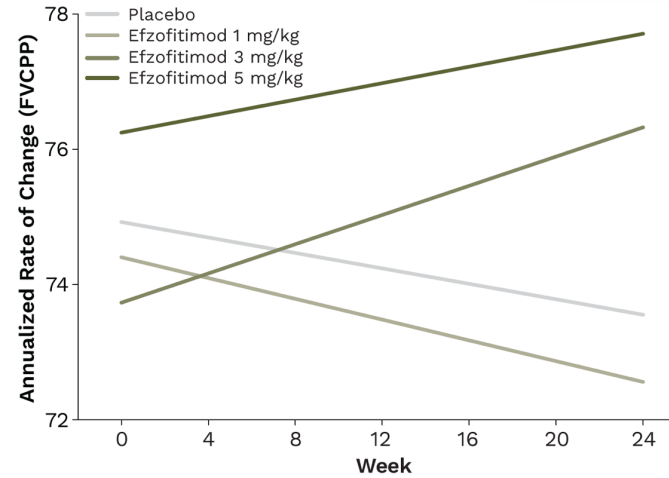


# Clinical Proof of Concept Demonstrated in Phase 1b/2a Pulmonary Sarcoidosis Trial

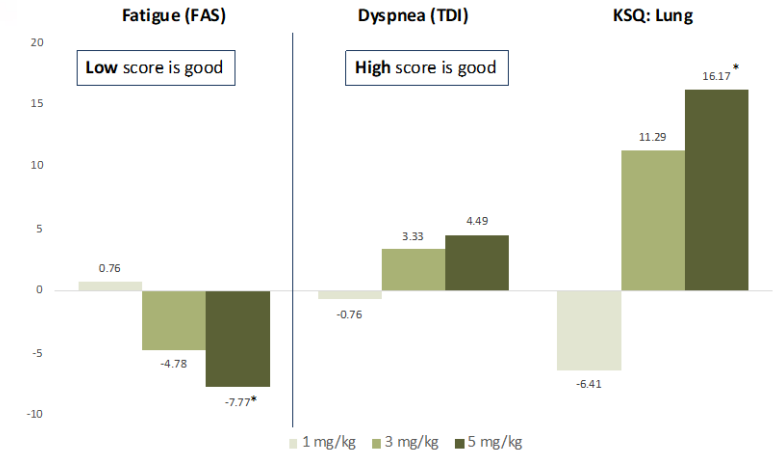
## Reduction in Avg Daily OCS vs Placebo\*



## Lung Function



## Symptom Improvement vs Placebo

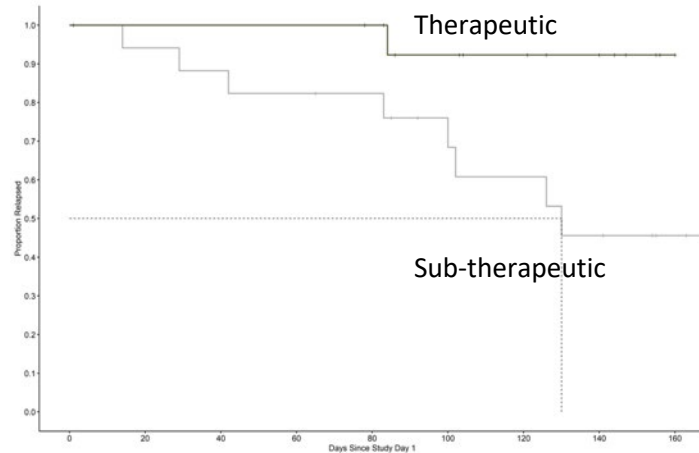


- Primary objective met: Efzofitimid was **safe and well-tolerated** (n=37)
- Secondary objectives met: **Dose-response observed** across all three families of pre-specified endpoints compared to placebo
- Dose-dependent **reduction of inflammatory biomarkers**
- Improvements in **time-to-first steroid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



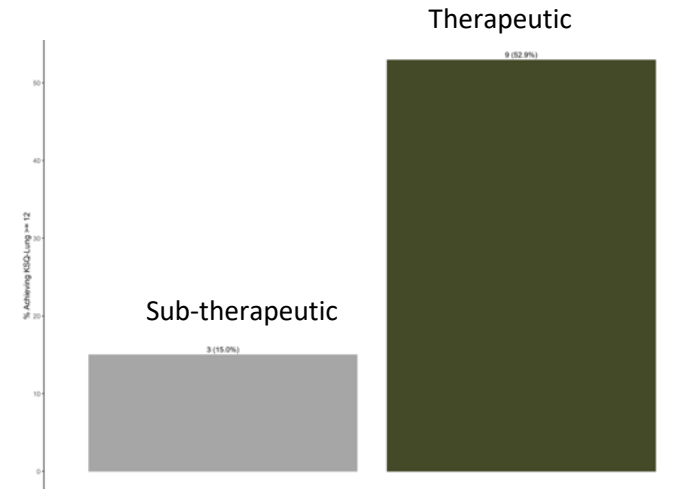
# Therapeutic Efzofitimod Doses Significantly Improve Multiple Efficacy Measures

## Time to first relapse of steroid taper




$p = 0.017$

## % Patients with KSQ-Lung $\geq 12$



$p = 0.032$

- 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

 **ERJ** open research THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

**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

**End-of-Phase 2 (EOP2) meeting with U.S. FDA conducted in Q122 aligned on prioritization of efficacy parameters**

## **Primary Endpoint — Steroid Reduction**

*Change from baseline in mean daily OCS dose post-taper*

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

## **Secondary Endpoint — FVC**

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

## **Secondary Endpoint — KSQ-Lung**

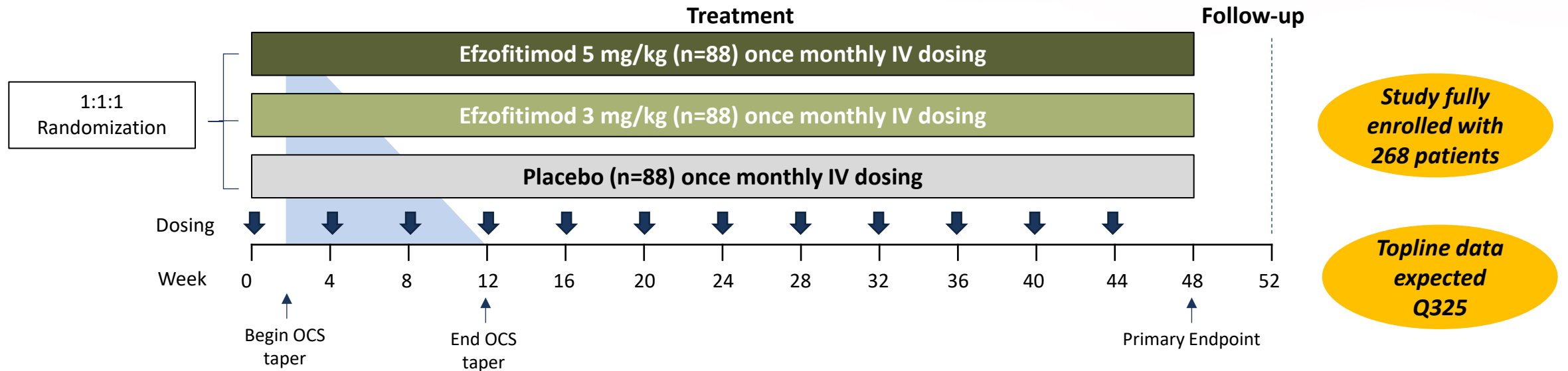
- The most relevant patient reported outcome indicative of disease specific pulmonary symptoms

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

# Global Phase 3 Trial in Pulmonary Sarcoidosis Ongoing



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



## Population: moderate to severe pulmonary sarcoidosis

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

## 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 efzofitimid outside of the clinical trial



SSc-ILD

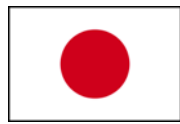
Indication Expansion Represents Upside  
Opportunity in Interstitial Lung Disease

# 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

## Epidemiology

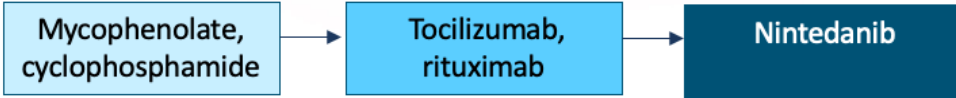


>1.5 million patients worldwide

## Diagnosis

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

## Current Treatments



- Efszofitimid positioned as 2<sup>nd</sup> line in patients who progress on or cannot tolerate MMF / CYC
- Addressable population in major markets: >50k<sup>(1)</sup>
- 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%**

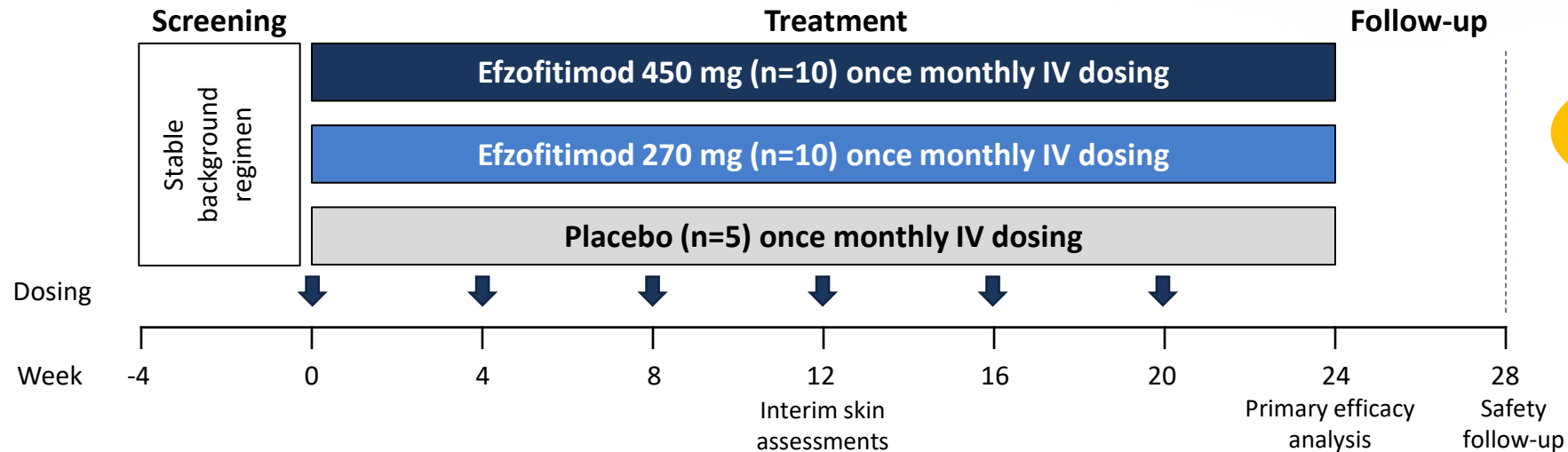
of ILD develops in the first three years of SSc



**30%**

of patients develop lung fibrosis

**Primary objective:** Assess the efficacy of efzofitimid 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.



**aTyr**

A New Approach to Interstitial Lung Disease

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

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

(1) In partnership with Kyorin Pharmaceutical Co., Ltd. for the development and commercialization of efzofitimid 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
- 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

- ~\$68.9m in cash, restricted cash, cash equivalents and investments as of Q324; additional \$19.4m in gross proceeds raised from at-the-market (ATM) offering subsequent to Q324
- Cash runway through filing of a Biologics License Agreement (BLA) for efzofitimod in pulmonary sarcoidosis
- Partnership with Kyorin Pharmaceutical for efzofitimod for ILD in Japan





Thank You