

The logo for aTyr, featuring the lowercase letter 'a' in a yellow-to-orange gradient, followed by 'Tyr' in a dark green color. The letters are in a bold, sans-serif font.

aTyr

A New Approach to Interstitial Lung Disease

January 2025

Forward Looking Statements

The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” “opportunity,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements regarding: the potential therapeutic benefits of proteins derived from tRNA synthetase genes and our product candidates and development programs; the ability to successfully advance our product candidates and undertake certain development activities (such as the initiation of clinical trials, clinical trial enrollment, the conduct of clinical trials and announcement of clinical results) and accomplish certain development goals, and the timing of such events; the potential market opportunity for our product candidates; our ability to receive regulatory approvals for, and commercialize, our product candidates; our ability to identify and discover additional product candidates; potential activities and payments under collaboration agreements; and the ability of our intellectual property portfolio to provide protection are forward-looking statements. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These risks, uncertainties and other factors are more fully described in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K, our subsequently filed Quarterly Reports on Form 10-Q, and in our other filings. The forward-looking statements in this presentation speak only as of the date of this presentation and neither we nor any other person assume responsibility for the accuracy and completeness of any forward-looking statement. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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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**

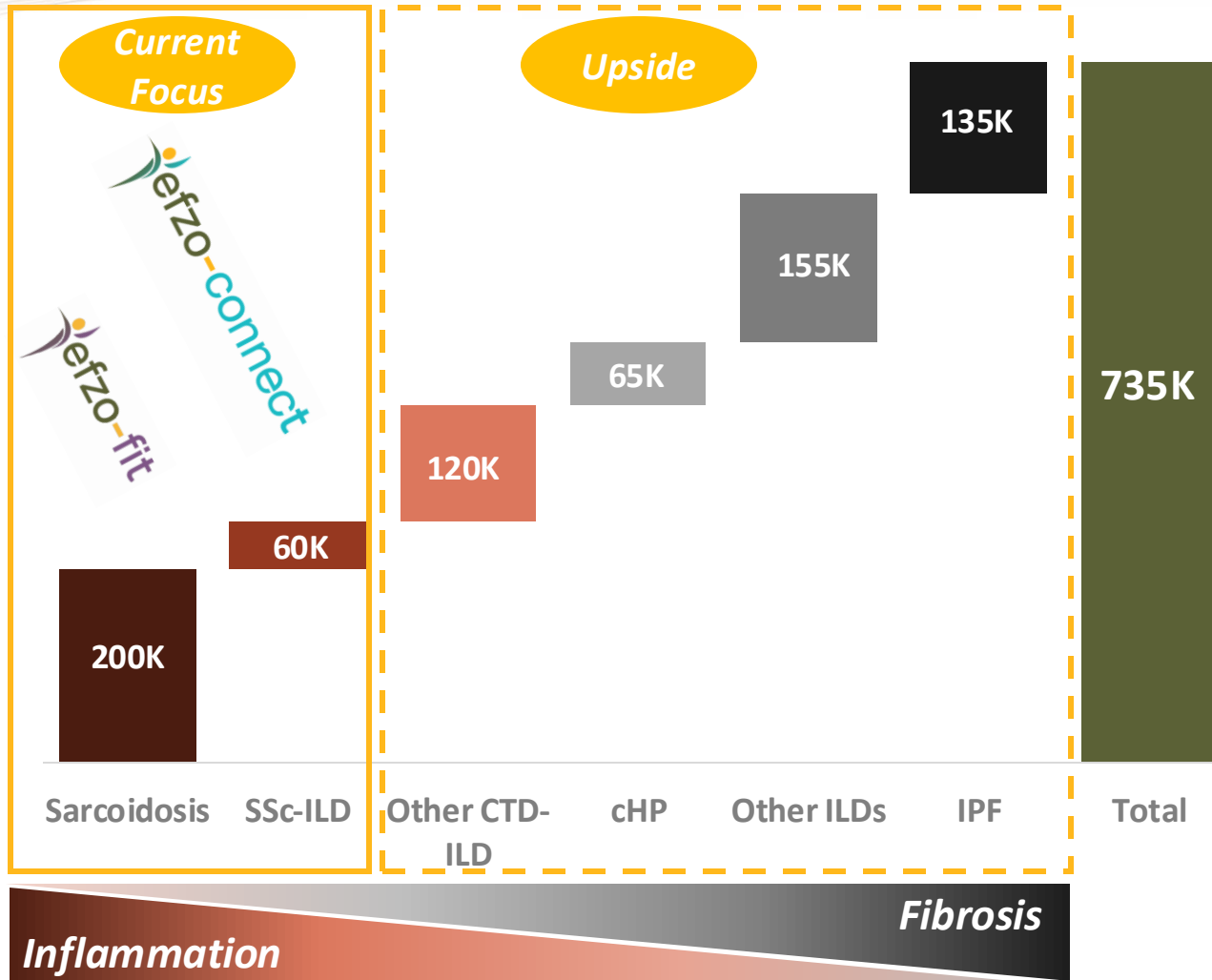


End stage fibrotic lung*

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

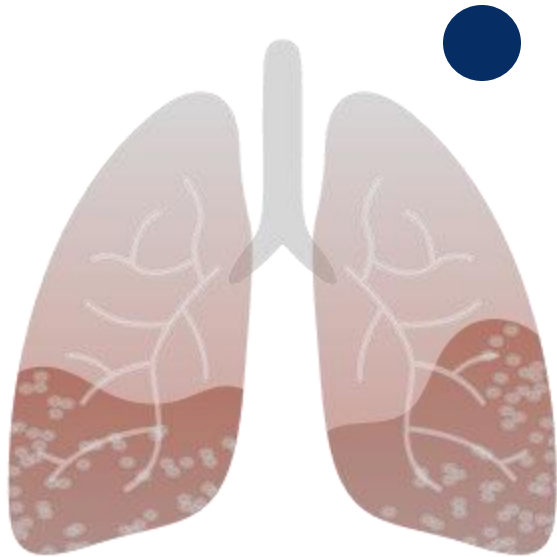
aTyr is Advancing Efzofitimid as the Standard-of-Care for ILD

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

Efzofitimod: First-in-Class Biologic Immunomodulator for ILD



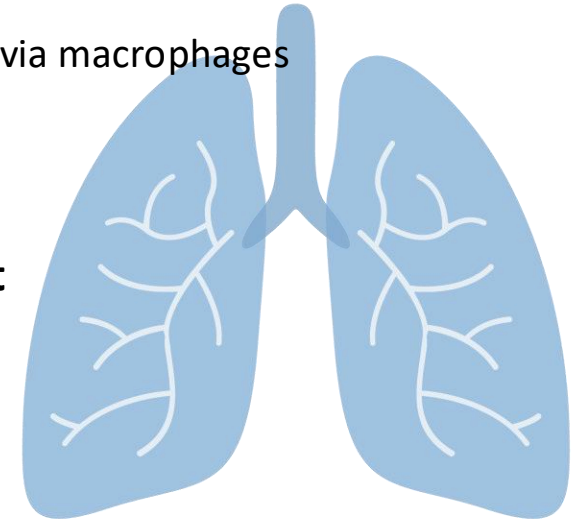
Targets innate immunity at site of inflammation

- 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

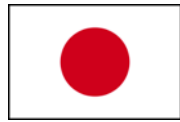
Epidemiology



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



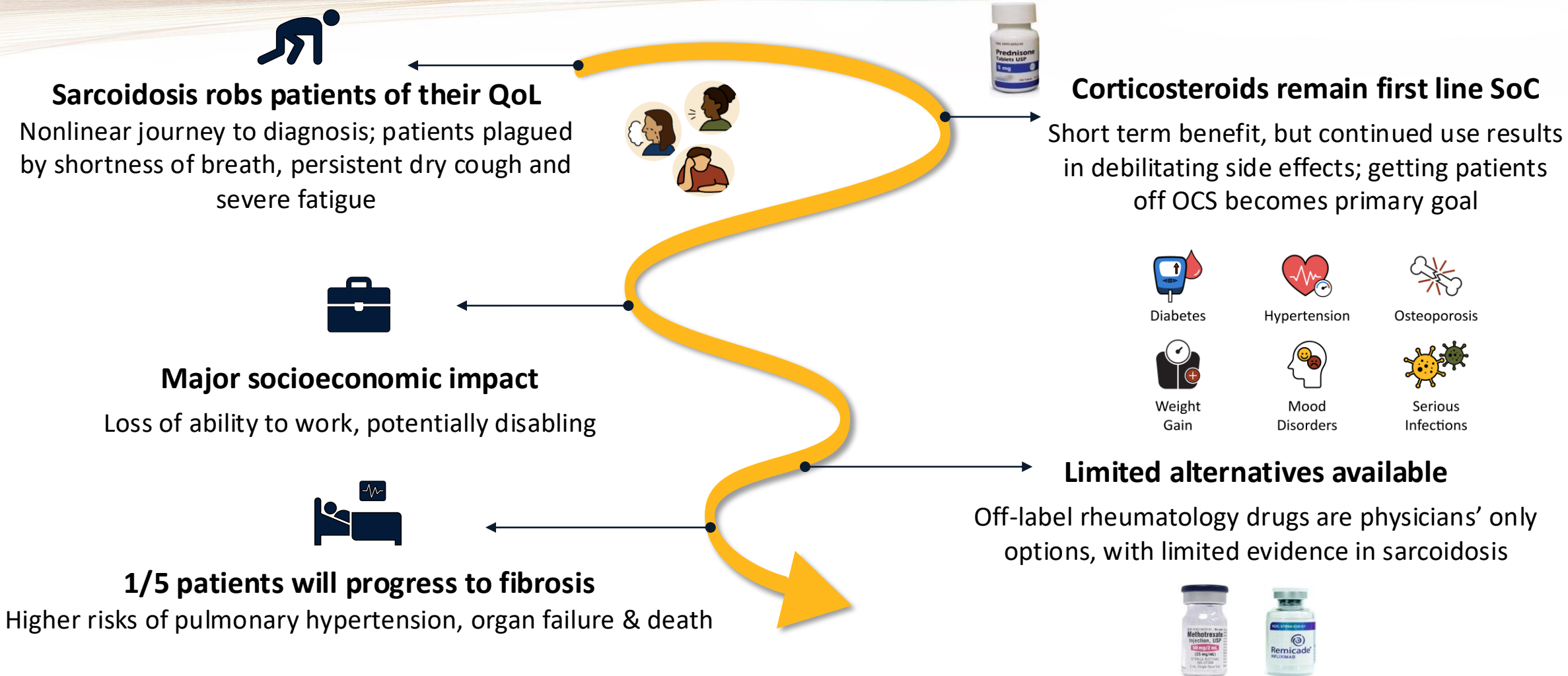
70%
of patients need
treatment within
first 3 years



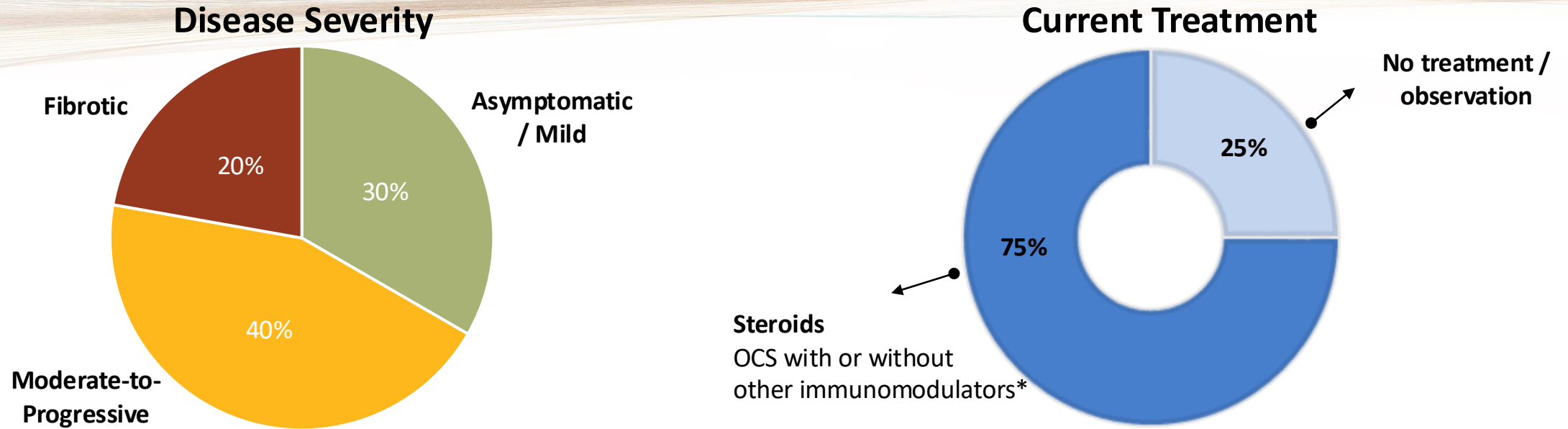
20%
of patients will
develop lung
fibrosis

- 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**⁽¹⁾

Multiple Benchmarks Support Premium Pricing for New Rare Disease Treatments

\$200K*



TAVNEOS
(avacopan)

Livdelzi
seladelpar

Nucala
(mepolizumab)

OFEV
nintedanib

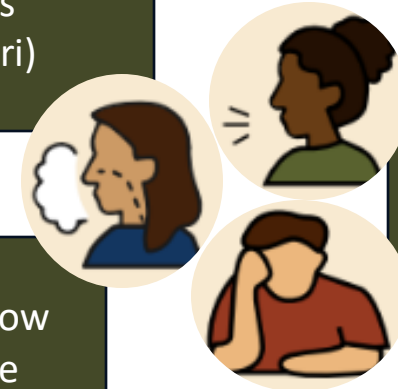
FILSPARI

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

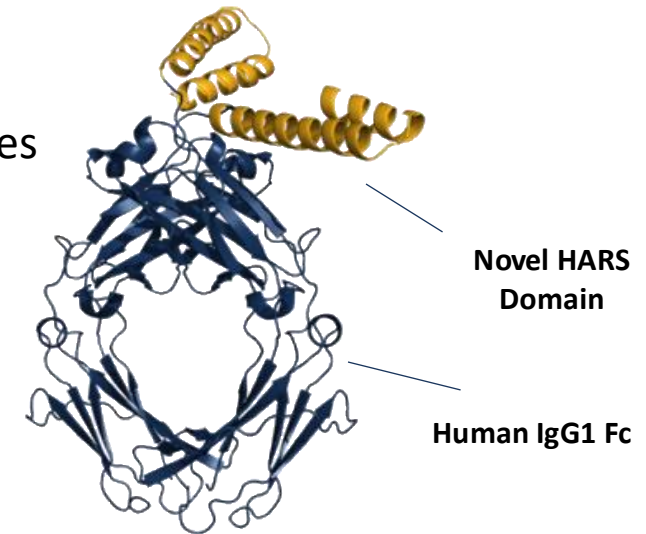
The logo for aTyr, featuring the lowercase letters 'aTyr' in a bold, sans-serif font. The 'a' is yellow, 'T' is dark green, and 'yr' is a lighter green. The background of the slide is a light green gradient with a series of thin, wavy lines in shades of yellow and green that sweep across the top and right side.

Efzofitimod

First-in-Class Biologic Immunomodulator for
Interstitial Lung Disease

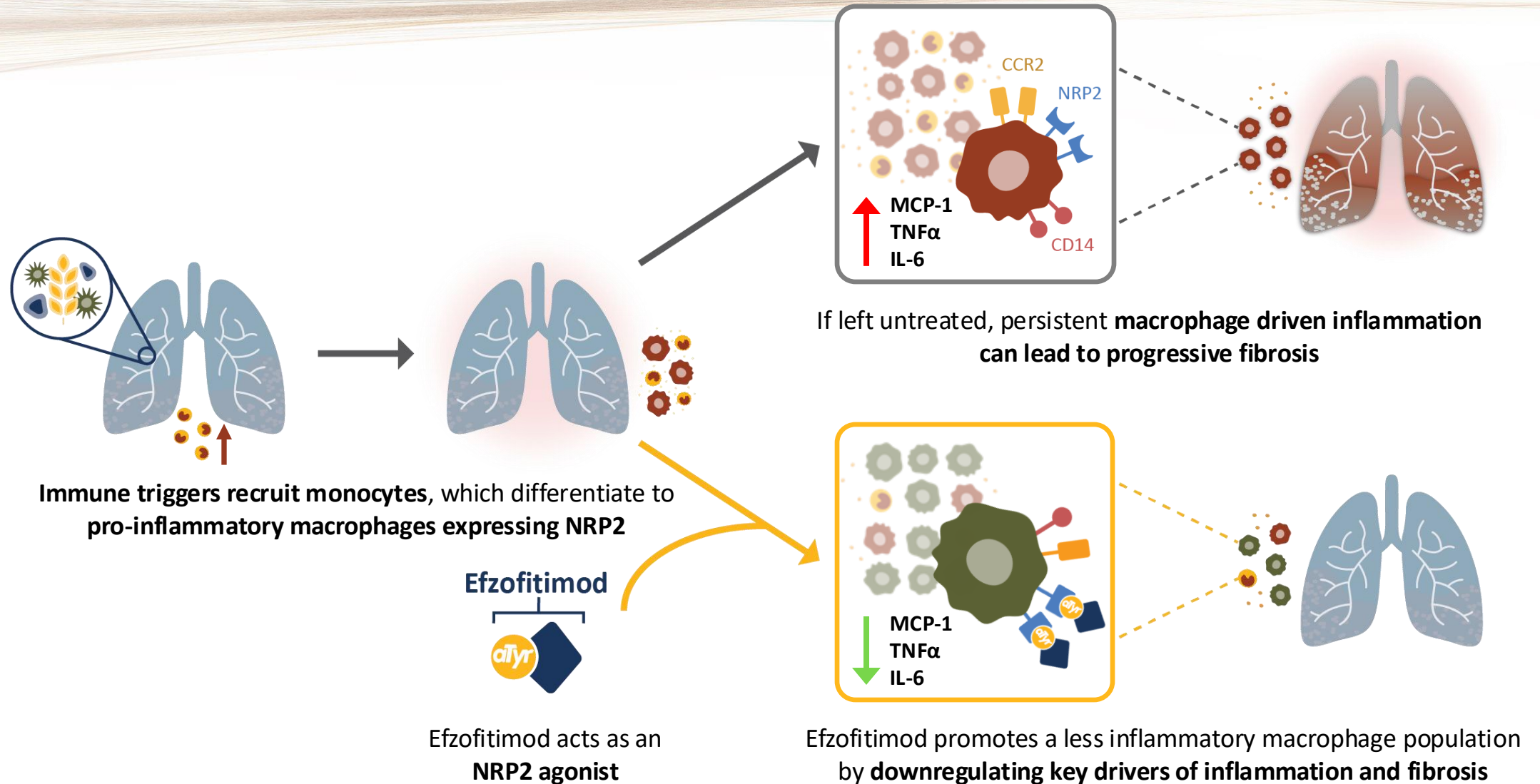
Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

- ✓ 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



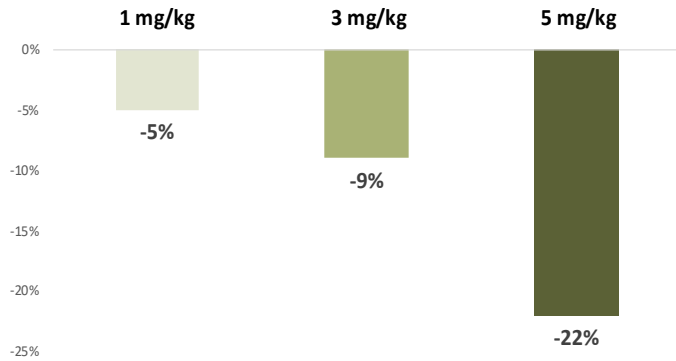
Predicted U.S. commercial exclusivity into 2039 based on composition of matter patents, with expected patent term extension and regulatory exclusivity programs

Efzofitimid Modulates Macrophages to Reduce Key Drivers of Inflammation & Fibrosis

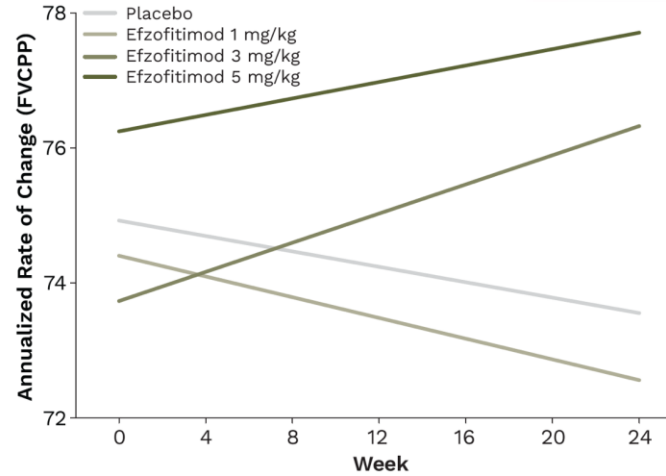


Clinical Proof of Concept Demonstrated in Phase 1b/2a Pulmonary Sarcoidosis Trial

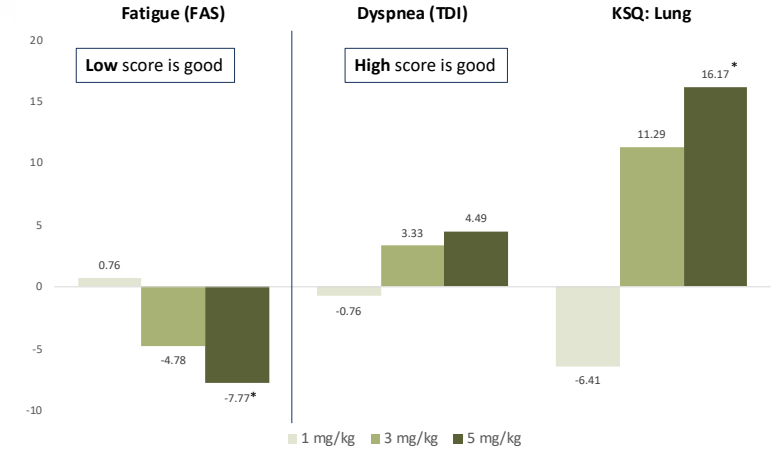
Reduction in Avg Daily OCS vs Placebo*



Lung Function



Symptom Improvement vs Placebo

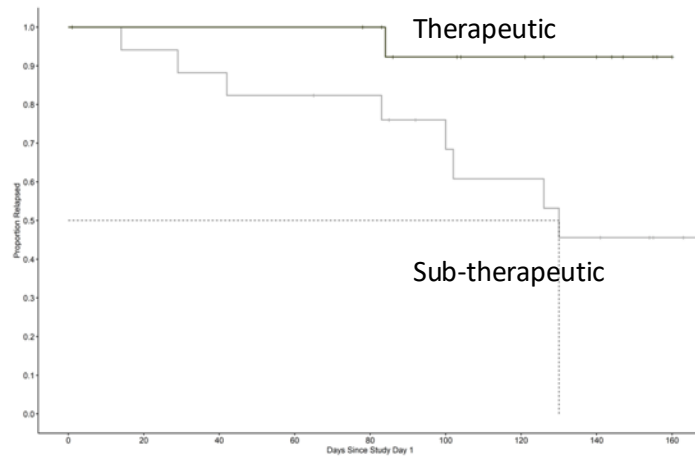


- Primary objective met: Efzofitimid was **safe and well-tolerated** (n=37)
- Secondary objectives met: **Dose-response observed** across all three families of pre-specified endpoints compared to placebo
- Dose-dependent **reduction of inflammatory biomarkers**
- Improvements in **time-to-first steroid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



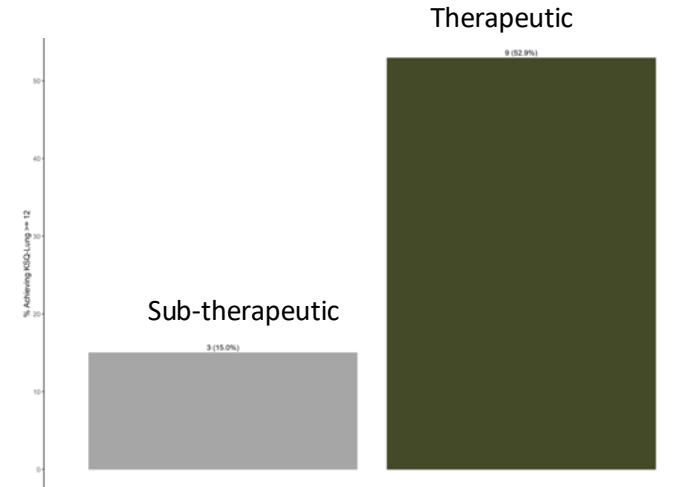
Therapeutic Efzofitimid Doses Significantly Improve Multiple Efficacy Measures

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 efzofitimid in pulmonary sarcoidosis
- Pooled analysis comparing 3.0 and 5.0 mg/kg efzofitimid (therapeutic group) vs 1.0 mg/kg efzofitimid and placebo (sub-therapeutic group)
- Improvements in **time-to-first steroid relapse** and **steroid relapse rate** for therapeutic efzofitimid doses

 THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Therapeutic Doses of Efzofitimid 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 Niranjana, 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

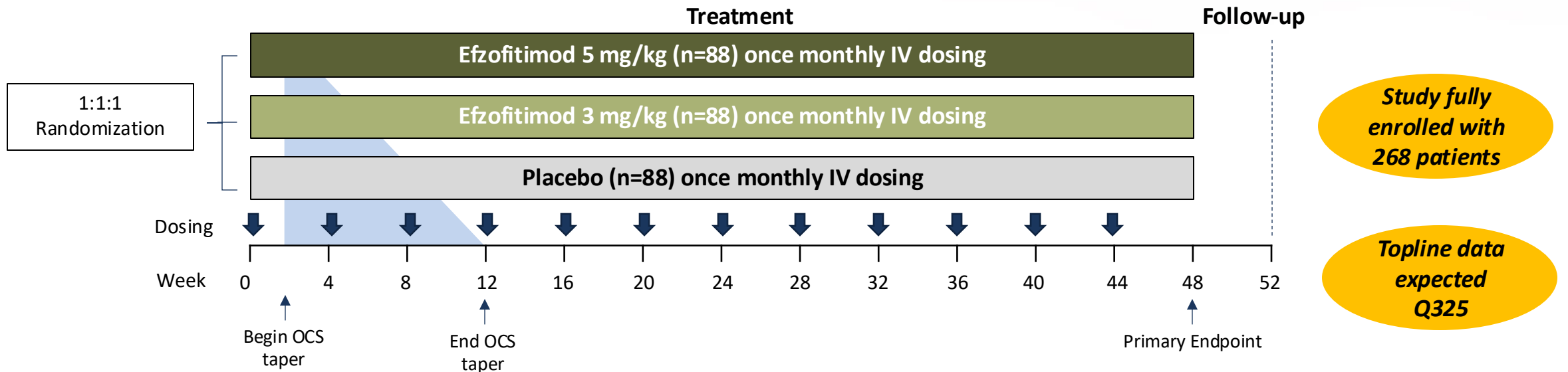
- The most relevant patient reported outcome indicative of disease specific pulmonary symptoms

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 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

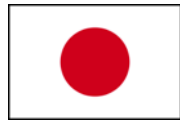
Indication Expansion Represents Upside
Opportunity in Interstitial Lung Disease

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

Epidemiology



>1.5 million patients worldwide

Diagnosis

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

Current Treatments

Mycophenolate,
cyclophosphamide

Tocilizumab,
rituximab

Nintedanib

- Ezosifitimid 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

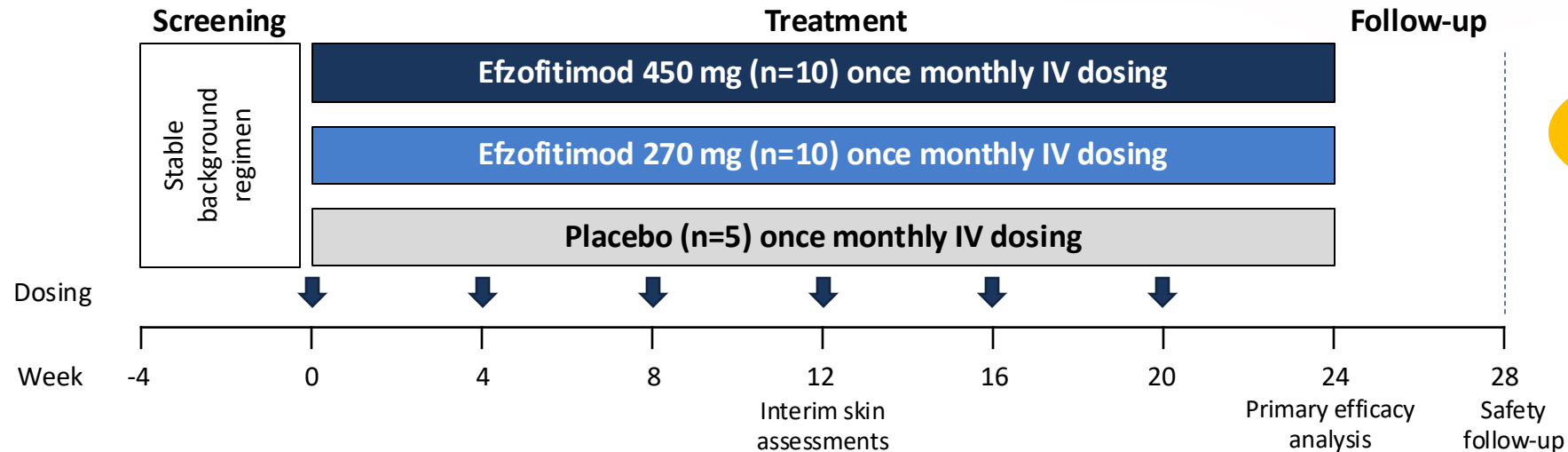


30%

of patients
develop lung
fibrosis

Phase 2 POC Trial Enrolling in SSc-ILD

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.



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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 ⁽¹⁾				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 ⁽²⁾							

(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





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Thank You