The Evolutionary Intelligence Biotech

March 2024

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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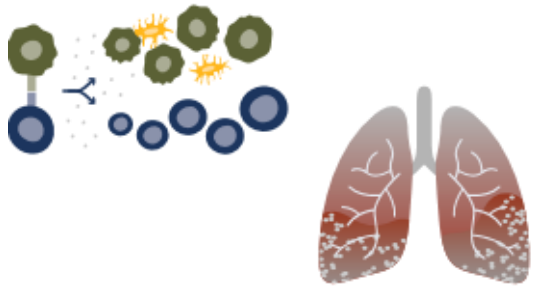
This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the uses for which they are being studied. 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.

Translating tRNA Synthetases into New Therapies for Fibrosis and Inflammation

Proprietary tRNA synthetase platform

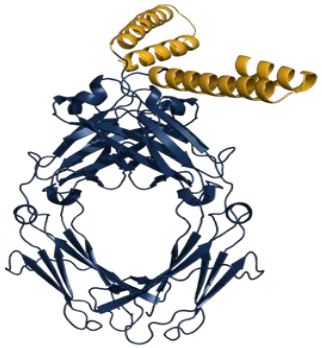
- Novel extracellular functions gained through evolutionary intelligence
- Potential new class of medicines
- IP directed to protein compositions from all 20 tRNA synthetase genes

Therapeutic focus: inflammation and fibrosis



- Vast therapeutic potential
- Differentiated approach
- Multiple blockbuster opportunities

Efzofitimod: first-in-class biologic immunomodulator for ILD



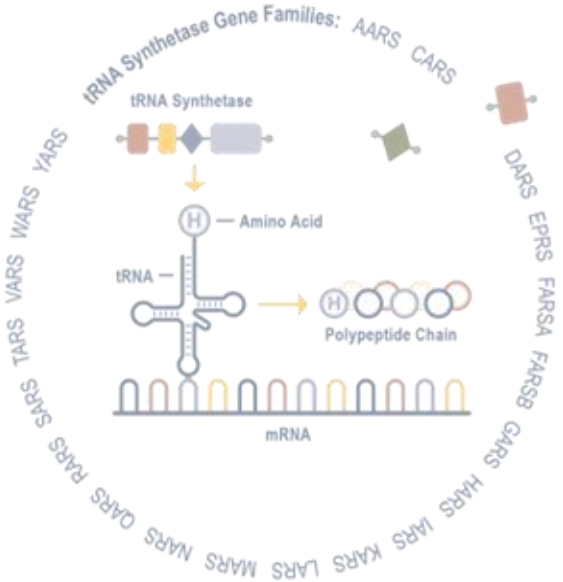
- Clinical proof of concept established
- Phase 3 EFZO-FIT™ study in pulmonary sarcoidosis expected to complete enrollment in Q224
- Phase 2 EFZO-CONNECT™ study in SSc-ILD enrolling

~$101.7m in cash, restricted cash, cash equivalents and investments as of December 31, 2023
Company projects cash runway through filing of Biologics License Application for efzofitimod in pulmonary sarcoidosis

Evolutionary Intelligence: tRNA Synthetases Evolved to Regulate Complex Systems

- **Novel tRNA synthetase domains evolved** as biology became more complex

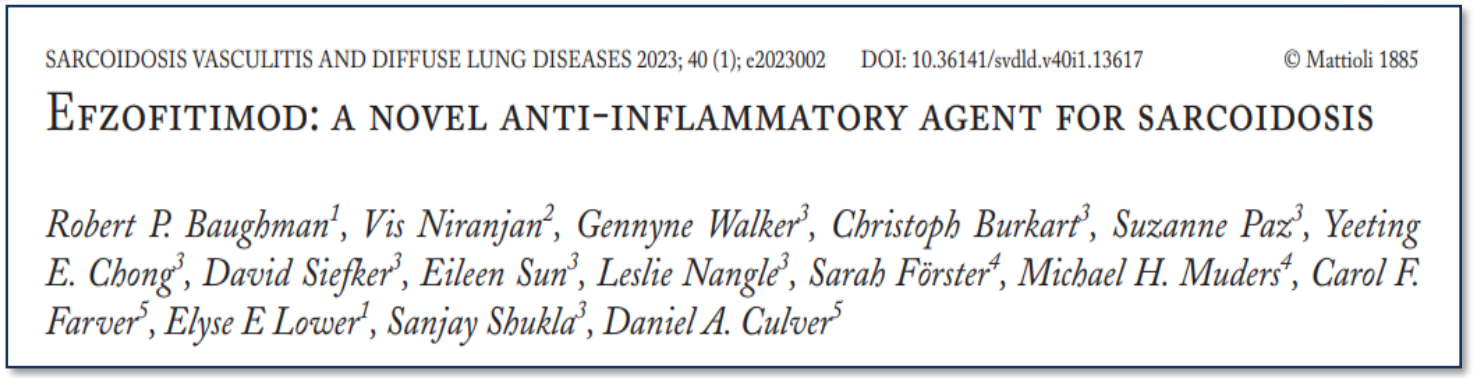
- Domains **persisted through evolutionary pressure**, indicating biological importance

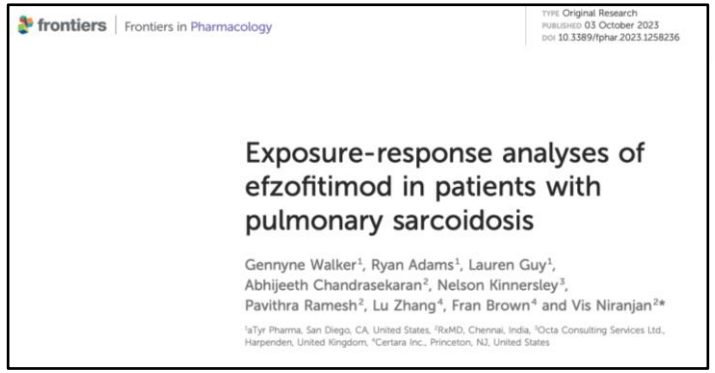


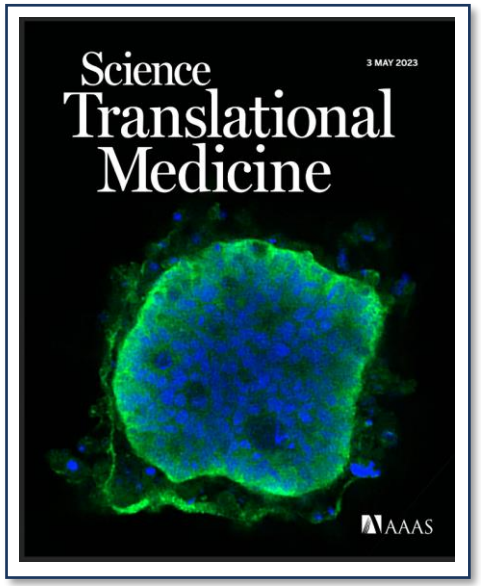
- Domains are **released locally** from full-length proteins enabling their function as **extracellular signaling molecules**

- Growing evidence that domains function to **restore homeostasis** through **new therapeutic intervention points** across multiple organ systems

Increasing Validation of aTyr Science in Peer Reviewed Journals







"Efzofitimod: a novel anti-inflammatory agent for sarcoidosis" – first major review article for efzofitimod (*https://doi.org/10.36141/svdld.v40i1.14396*); "Efzofitimod for the treatment of pulmonary sarcoidosis" – Phase 1b/2a data publication (*https://doi.org/10.1016/j.chest.2022.10.037*); "Exposure-response analyses of efzofitimod in patients with pulmonary sarcoidosis" – from Phase 1 and 1b/2a studies (*https://doi.org/10.3389/fphar.2023.1258236*); ATYR2810's target NRP2 biology on cover of *Science Translational Medicine* (*https://www.science.org/doi/10.1126/scitranslmed.adf1128*)

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			**ODD, Fast Track**
			SSc-ILD	efzo-connect			**ODD, Fast Track**
			Other ILD (CTD-ILD; CHP)				
ATYR0101	DARS	LTBP1 modulator	Fibrosis				
ATYR0750	AARS	FGFR4 modulator	Liver Disorders				
tRNA Synthetase Candidates(2)							

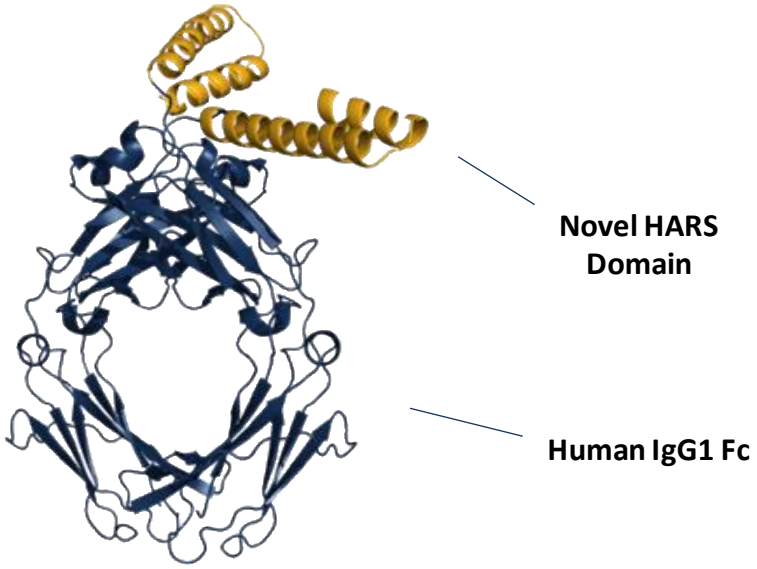
(1) In partnership with Kyorin Pharmaceutical Co., Ltd. for the development and commercialization of efzofitimod for ILD in Japan
(2) Pipeline candidates in development based on additional tRNA synthetases from IP portfolio
ODD = orphan drug designation; SSc-ILD = Scleroderma-related ILD; CTD-ILD = Connective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

Efzofitimod

First-in-Class Biologic Immunomodulator for Interstitial Lung Disease (ILD)

Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

- Fc fusion protein
- Active domain is naturally occurring, lung enriched domain of HARS
- Downregulates activated myeloid cells via NRP2
- Anti-inflammatory and anti-fibrotic effects demonstrated in multiple ILD models
- Dosed once-monthly via 60 minute IV infusion
- Clinical proof of concept demonstrated in pulmonary sarcoidosis

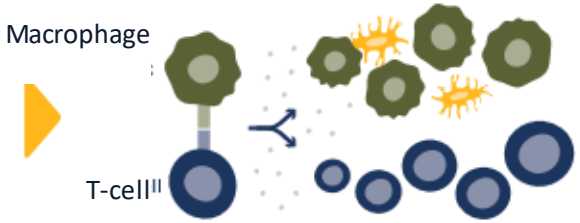


HARS = histidyl-tRNA synthetase
NRP2 = neuropilin-2

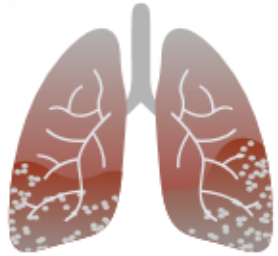
Efzofitimod Therapeutic Hypothesis: Restore Immune Balance to Prevent Fibrosis

ILDs share common immune pathology that can lead to progressive fibrosis

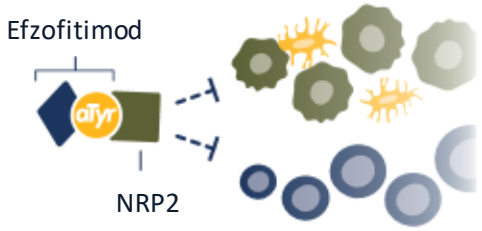
Diverse immune triggers activate common immune pathways



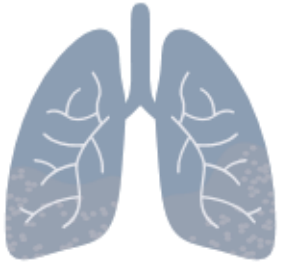
NRP2 upregulated on activated myeloid cells* – upstream of other targets



Chronic inflammation can lead to progressive fibrosis



Efzofitimod targets innate immunity to resolve inflammation without immune suppression



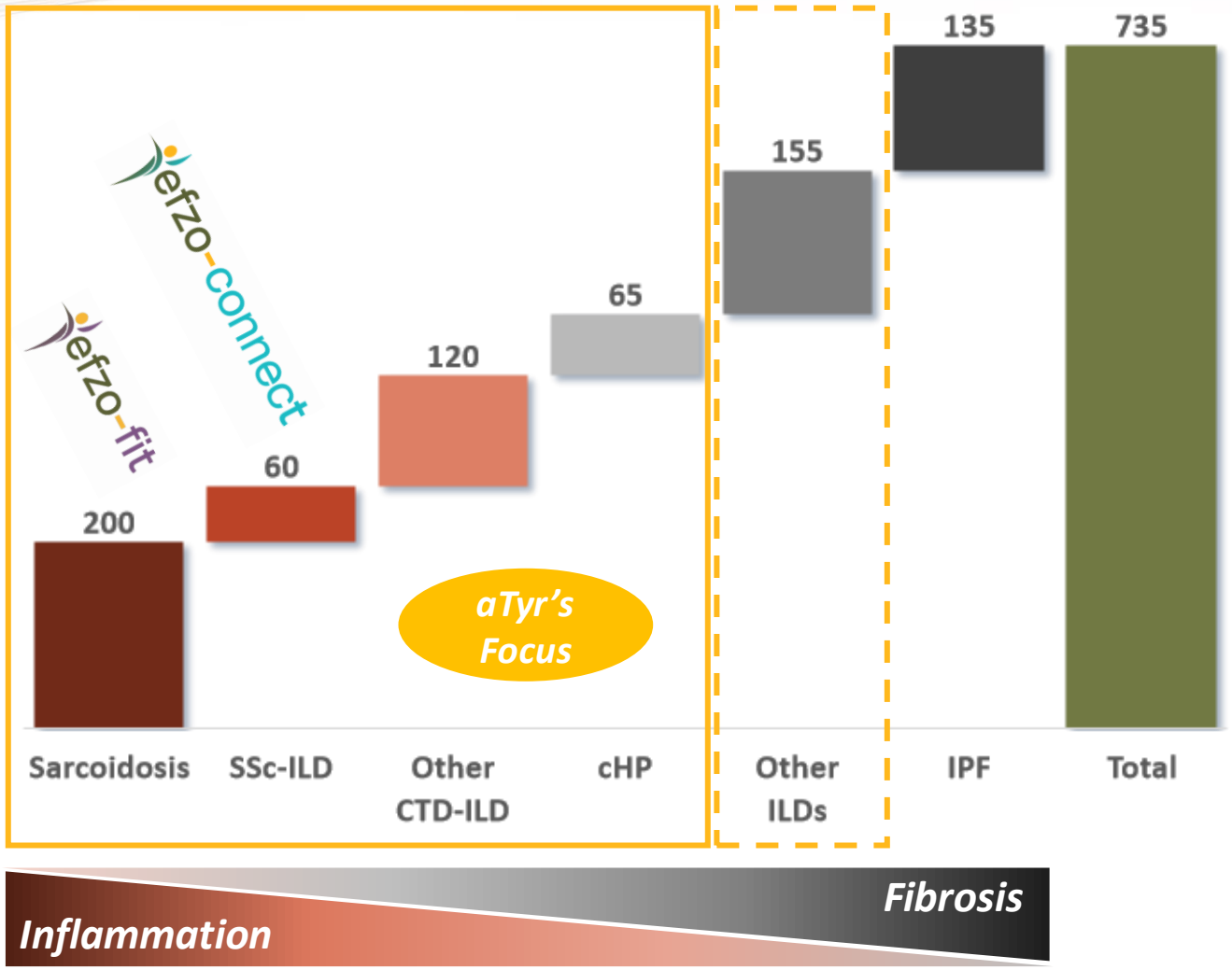
Therapeutic goal: Restore immune balance to **improve lung function, resolve symptoms** and **prevent disease progression**

*NRP2 also present on fibroblasts

Baughman et al. Efzofitimod: A Novel Anti-inflammatory Agent for Sarcoidosis. *Sarc Vasc And Diff Lung Dis.* 2023

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

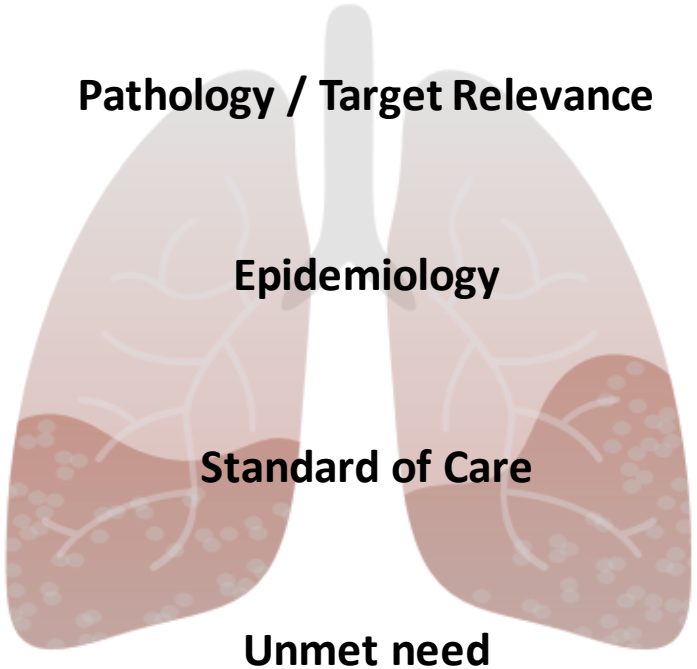
Number of U.S. ILD Patients by Types ('000)



- ILD is an umbrella term for >200 types of rare lung diseases that span a spectrum of inflammation and fibrosis
- Patients experience high morbidity and mortality
- No disease-modifying therapies available; current options have significant toxicities
- aTyr's focus estimated at $2-3B global market opportunity
- Upside potential in other ILD and related autoimmune diseases (e.g., SSc, lupus, RA)

(1) aTyr internal estimates

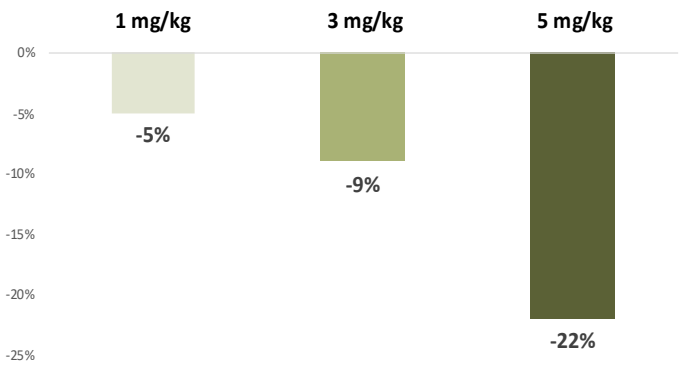
Significant Market Opportunity in Pulmonary Sarcoidosis Alone



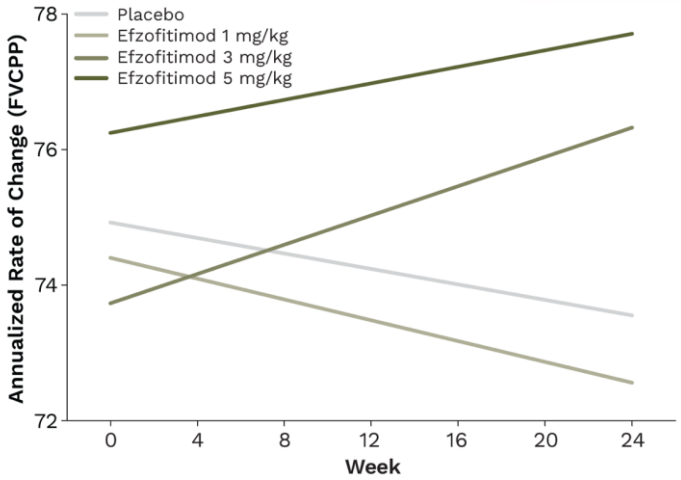
	Pulmonary Sarcoidosis
Pathology / Target Relevance	• Inflammatory disease characterized by non-caseating granulomas • NRP2 upregulated in sarcoid granulomas
Epidemiology	• 200K pts in the U.S.; >1M globally • Lung predominant in >90% • Up to 20% develop lung fibrosis
Standard of Care	• Oral corticosteroids (OCS) (50-75% of patients) • Immunosuppressants (30% of patients) • anti-TNF antibodies (10% of patients)
Unmet need	• No disease modifying therapies available • Significant toxicity with current treatment options
Efzofitimod Positioning	• 1st line as steroid sparing agent • Avoid current 2nd / 3rd line therapies

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

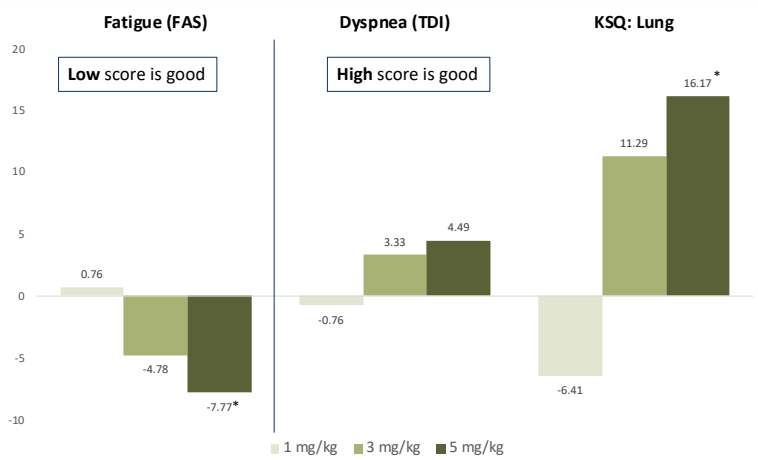
Steroid Sparing



Lung Function



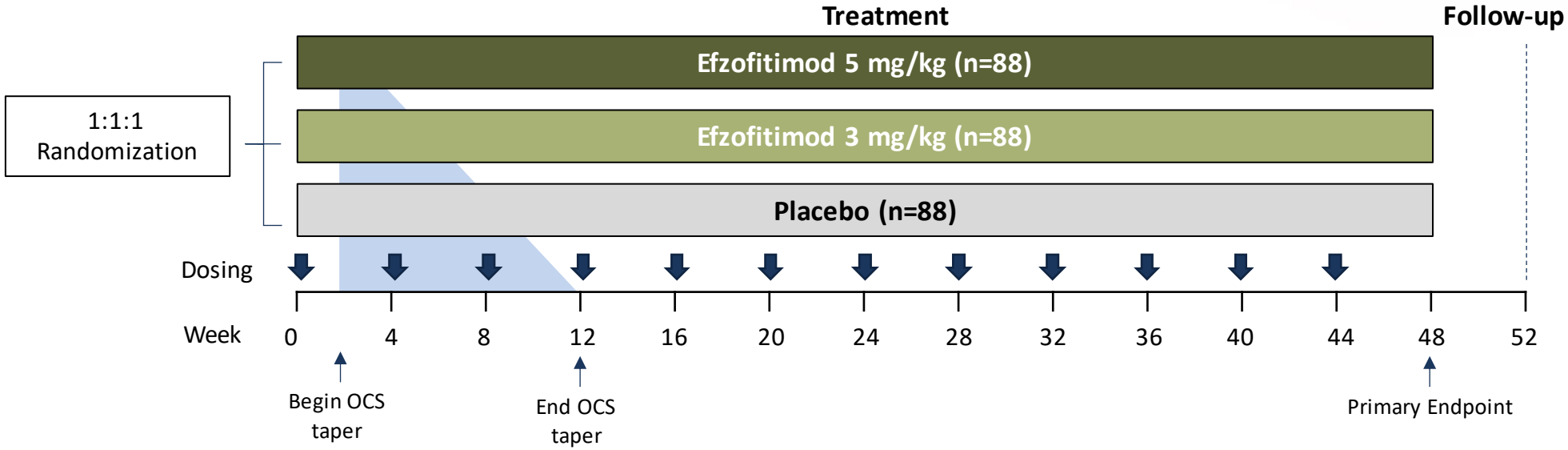
Symptom Control



- 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
- Dose-dependent **improvement of inflammatory biomarkers**
- **Robust results**: Pre-specified analysis plan, trends consistent across analysis populations and imputation methods

Global Phase 3 Trial Enrolling in Pulmonary Sarcoidosis

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%

Primary Endpoint

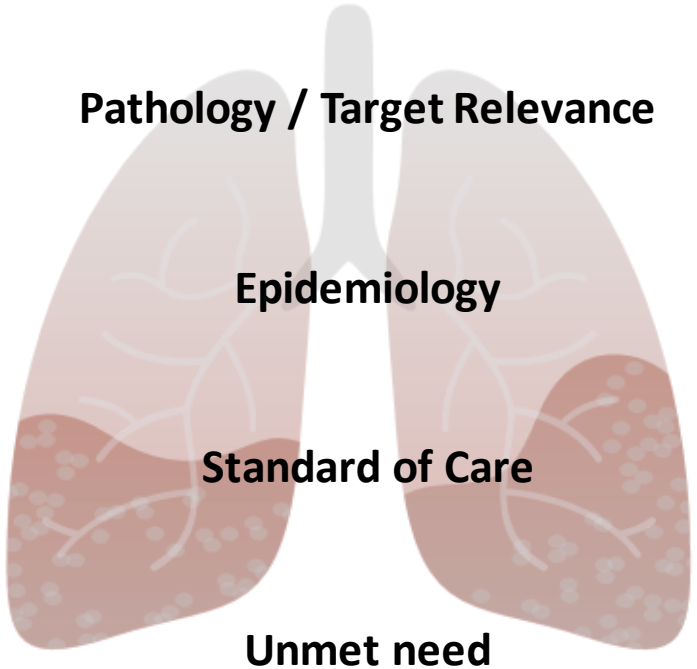
- Steroid burden: change in daily steroid dose

Key Secondary Endpoints

- Lung function: forced vital capacity
- Symptom control: KSQ-Lung score

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

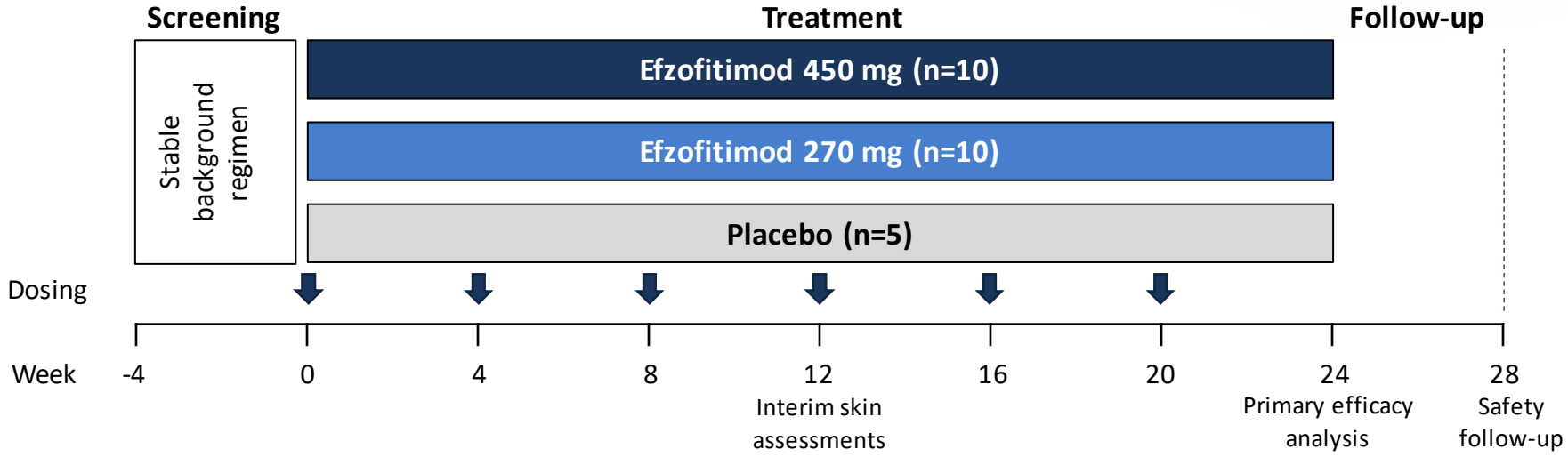
SSc-ILD Represents Expanded Commercial Opportunity



	SSc-ILD
Pathology / Target Relevance	• Lung manifestation of systemic sclerosis (SSc), an autoimmune disease characterized by scarring of skin and other organs • NRP2 upregulated in skin macrophages
Epidemiology	• >60K in the U.S.; >1.5M globally • 25-30% develop lung fibrosis
Standard of Care	• Mycophenolate (MMF) (80% of pts in U.S.) • Cyclophosphamide (CYC) • Rituximab; nintedanib; tocilizumab
Unmet need	• No disease modifying therapies available • Significant toxicity with current treatment options
Efzofitimod Positioning	• 2nd line in pts not controlled on MMF / CYC • 1st line to replace MMF / CYC

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

Primary Endpoint

- Lung function: forced vital capacity

Key Secondary Endpoints

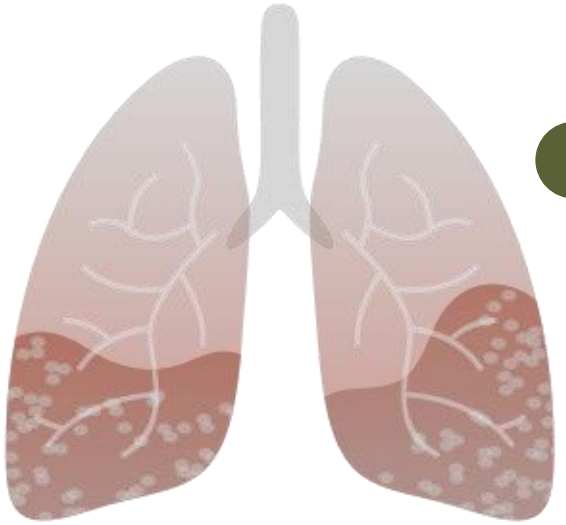
- Symptom control: PROs
- Skin: histopathology, gene profiling, biomarkers, mRSS

Study designed in collaboration with leading SSc-ILD physicians in the U.S.: **Kristin Highland, MD**, Cleveland Clinic; **Shervin Assassi, MD**, University of Texas, Houston

POC = Proof of Concept

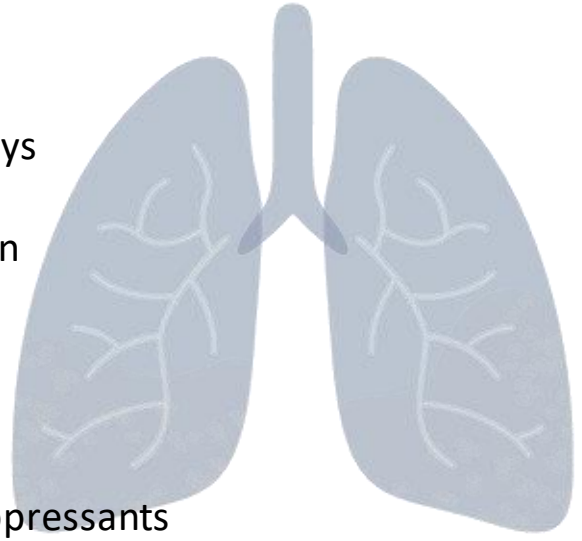
Efzofitimod Target Value Proposition

Binds new target for ILD
- upstream
- not repurposed or failed



Targets innate immunity at site of inflammation
- downregulates pro-inflammatory and pro-fibrotic pathways
- addresses complex immune pathology
- restores immune balance without evidence of suppression

Robust efficacy
- Improves lung function
- Resolves symptoms
- Reduces OCS or other immune suppressants



No known safety issues

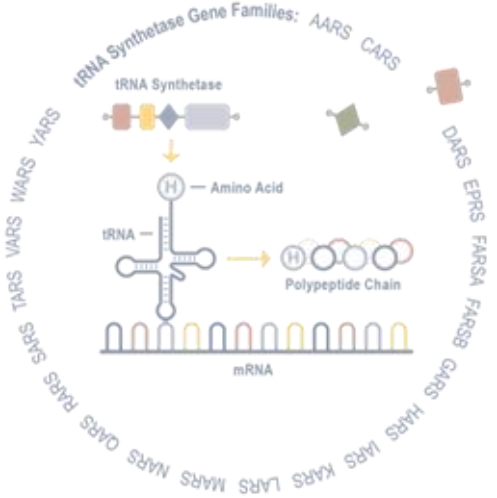
Pre-Clinical Pipeline

Generating New Treatments for Inflammation and Fibrosis

tRNA Synthetase Platform

Unique drug discovery platform leveraging evolutionary intelligence

- Extracellular tRNA synthetases can unlock new targets and / or signaling pathways
- Low bias towards biology or indication



Approach validated through efzofitimod clinical POC

- HARS derived NRP2 modulator efzofitimod currently in Phase 3 in pulmonary sarcoidosis

Pipeline of candidates targeting high-value markets

- Differentiated MoAs could potentially lead to superior results vs. SOC
- Selectively target activated systems

Deep research capabilities with a proprietary molecule library

- IP directed to protein compositions from all 20 tRNA synthetase genes
- Research Collaboration with Dualsystems Biotech AG aims to identify target receptors for tRNA synthetases

Translating tRNA Synthetase Biology into New Therapies for Inflammation and Fibrosis

Translating tRNA Synthetases into New Therapies for Inflammation and Fibrosis

Evolutionary intelligence drug discovery platform

- Extracellular tRNA synthetases represent potential new class of medicines
- aTyr owns IP directed to entire class

Lead program in pivotal development for untapped blockbuster markets

- Clinical POC established in pulmonary sarcoidosis
- Global Phase 3 EFZO-FIT™ study in pulmonary sarcoidosis expected to complete enrollment in Q224
- Expansion to second indication with Phase 2 EFZO-CONNECT™ study enrolling in SSc-ILD

Growing pipeline of tRNA synthetase derived candidates

- Multiple next-generation programs targeting inflammation and fibrosis
- Unlocking new therapeutic intervention points

Robust financial position through multiple inflection points

- ~$101.7m in cash, restricted cash, cash equivalents and investments as of December 31, 2023
- Company projects cash runway through filing of BLA for efzofitimod in pulmonary sarcoidosis
- $175m partnership for efzofitimod in Japan with Kyorin Pharmaceutical

Thank You