



The Evolutionary Intelligence Biotech

H.C. Wainwright 25th Annual Global Investment Conference

Jill Broadfoot, CFO

September 13, 2023

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.

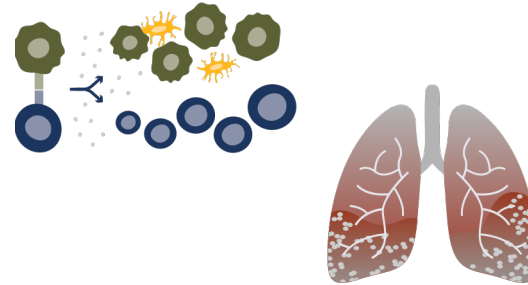
Translating tRNA Synthetases into New Therapies for Fibrosis and Inflammation

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

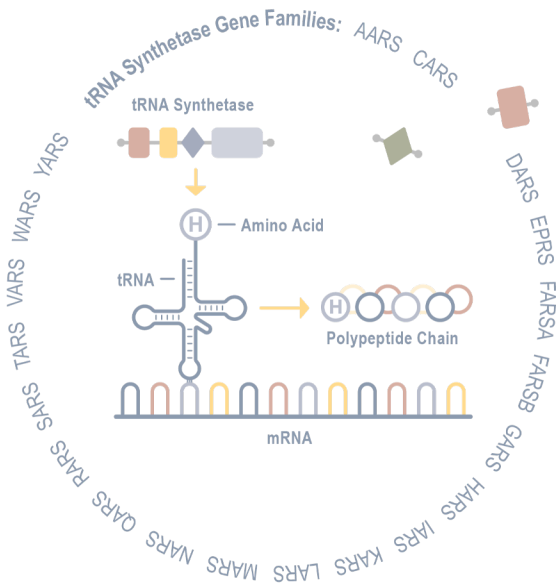


- Clinical proof of concept established
- Phase 3 EFZO-FIT™ study in pulmonary sarcoidosis enrolling
- Phase 2 EFZO-CONNECT™ study in SSc-ILD expected to initiate in Q3 2023

~\$112.0m in cash, restricted cash, cash equivalents and investments as of June 30, 2023
Company projects cash runway into 2026

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

SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2023; 40 (1); e2023002 DOI: 10.36141/svdld.v40i1.13617 © Mattioli 1885

EFZOFITIMOD: A NOVEL ANTI-INFLAMMATORY AGENT FOR SARCOIDOSIS

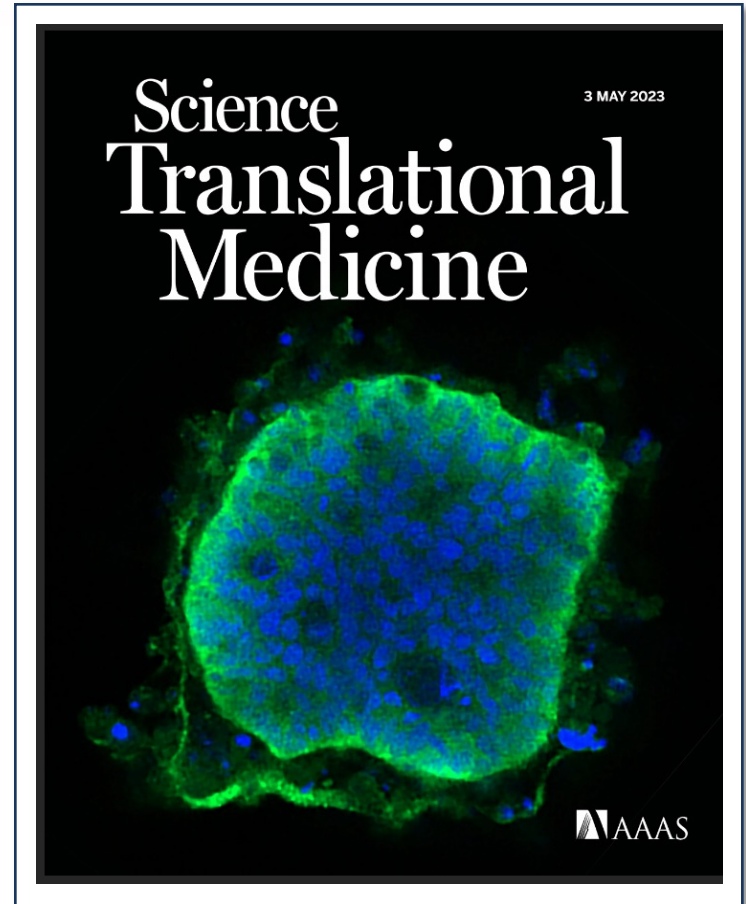
Robert P. Baughman¹, Vis Niranjan², Gennyne Walker³, Christoph Burkart³, Suzanne Paz³, Yeeting E. Chong³, David Siefker³, Eileen Sun³, Leslie Nangle³, Sarah Förster⁴, Michael H. Muders⁴, Carol F. Farver⁵, Elyse E Lower¹, Sanjay Shukla³, Daniel A. Culver⁵

 **CHEST**[®] JOURNAL

DIFFUSE LUNG DISEASE: ORIGINAL RESEARCH | ARTICLES IN PRESS

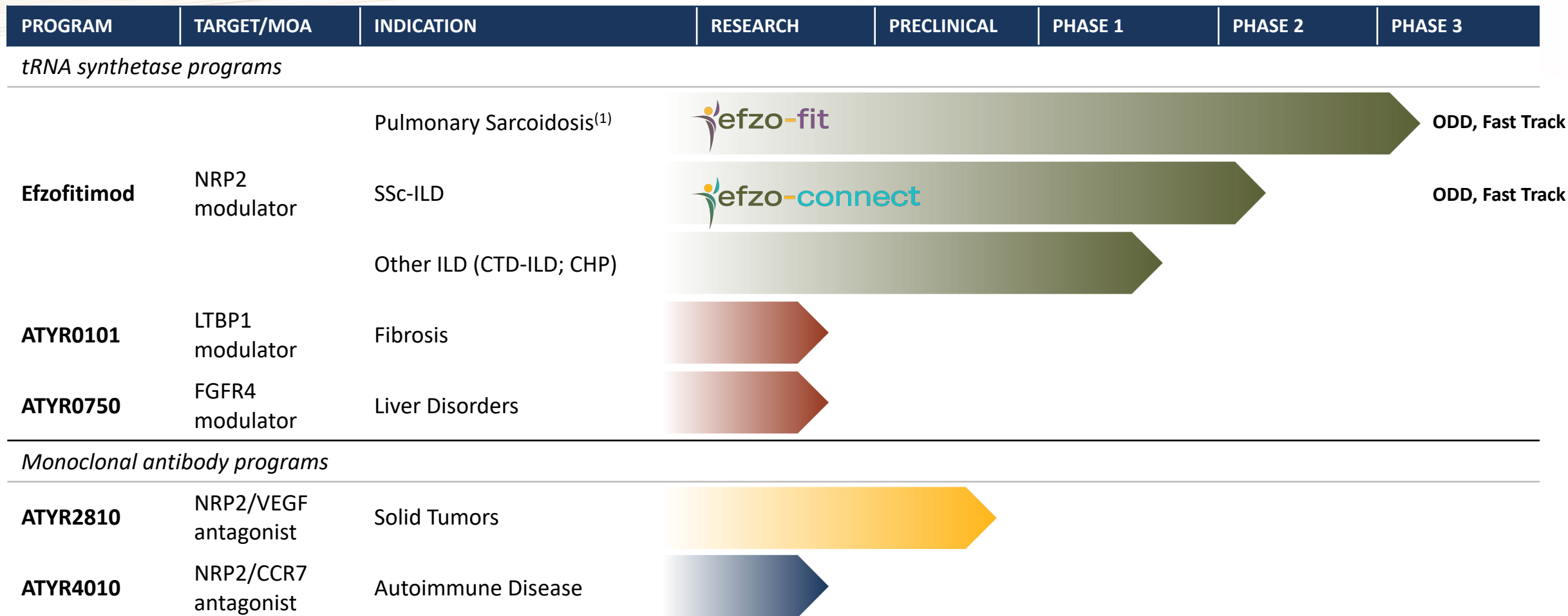
Efzofitimid for the Treatment of Pulmonary Sarcoidosis

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



“Efzofitimid: a novel anti-inflammatory agent for sarcoidosis” – first major review article for efzofitimid (<https://doi.org/10.36141/svdld.v40i1.14396>); “Efzofitimid for the treatment of pulmonary sarcoidosis” – Phase 1b/2a data publication (<https://doi.org/10.1016/j.chest.2022.10.037>); ATYR2810’s target NRP2 biology featured on the cover of *Science Translational Medicine* (<https://www.science.org/doi/10.1126/scitranslmed.adf1128>)

Growing Pipeline of First-in-Class tRNA Synthetase Derived Biologics



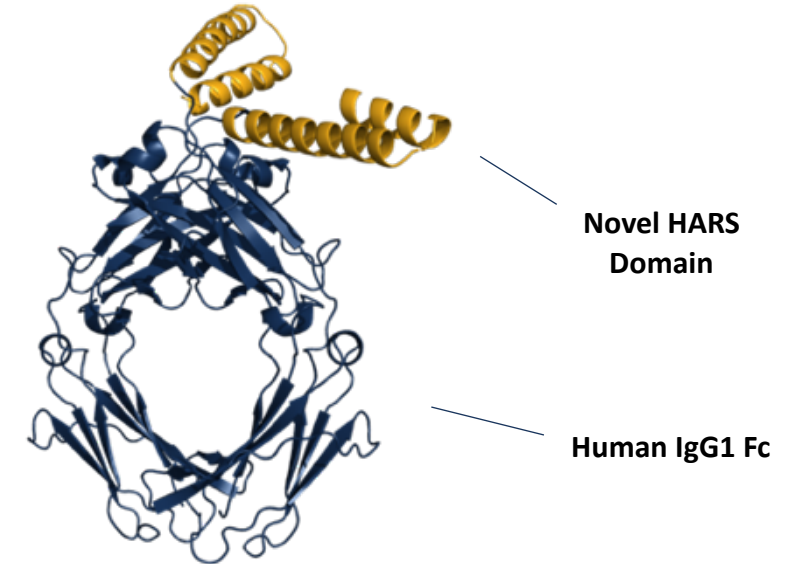


Efzofitimod

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

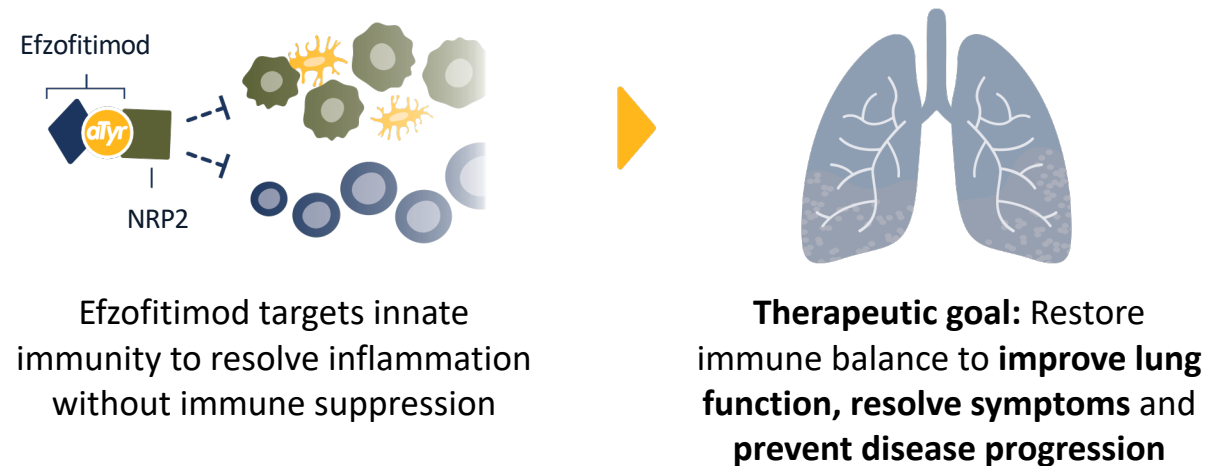
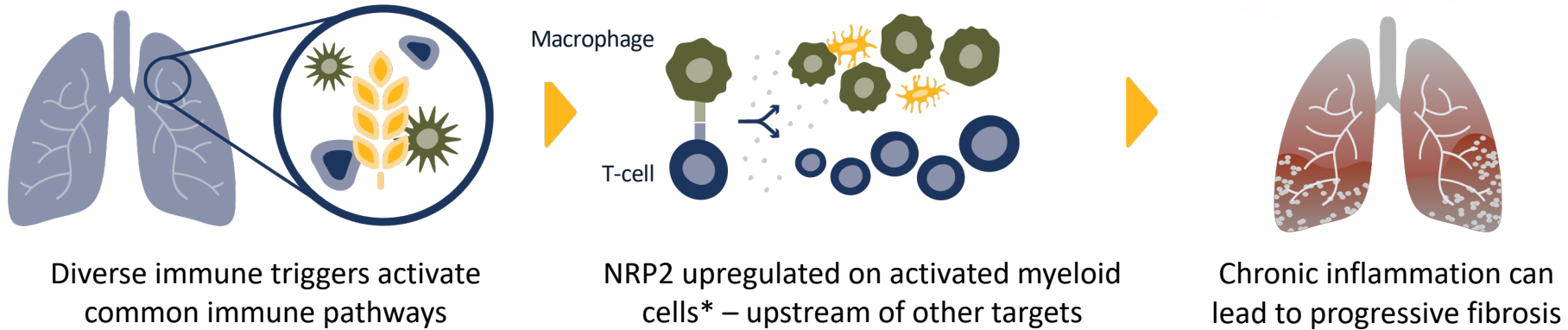
Efzofitimod: First-in-Class Biologic Immunomodulator for ILD

- 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



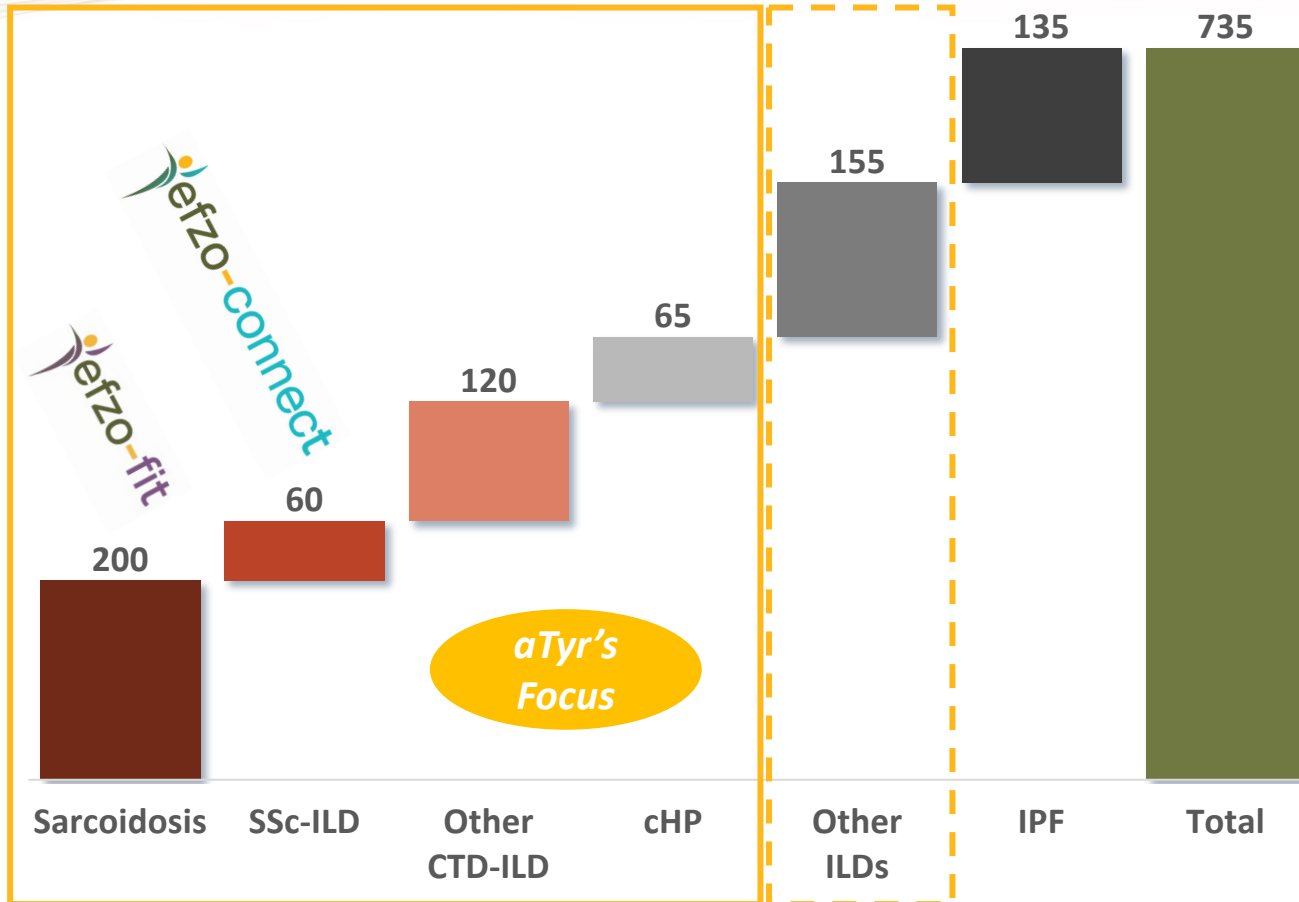
Efzofitimod Therapeutic Hypothesis: Restore Immune Balance to Prevent Fibrosis

ILDs share common immune pathology that can lead to progressive fibrosis



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

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

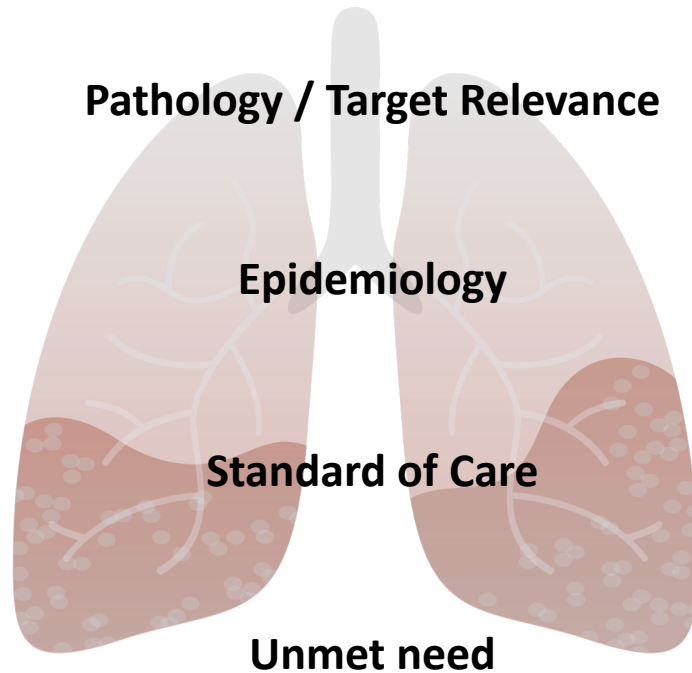


- ILD is an umbrella term for >200 types of rare lung diseases that span a spectrum of inflammation and fibrosis
- Patients experience high morbidity and mortality
- No disease-modifying therapies available; current options have significant toxicities
- aTyr's focus estimated at \$2-3B global market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

Inflammation

Fibrosis

Significant Market Opportunity in Pulmonary Sarcoidosis Alone



Efzofitimod Positioning

Pulmonary Sarcoidosis

- Inflammatory disease characterized by non-caseating granulomas
- NRP2 upregulated in sarcoid granulomas

- 200K pts in the U.S.; >1M globally
- Lung predominant in >90%
- Up to 20% develop lung fibrosis

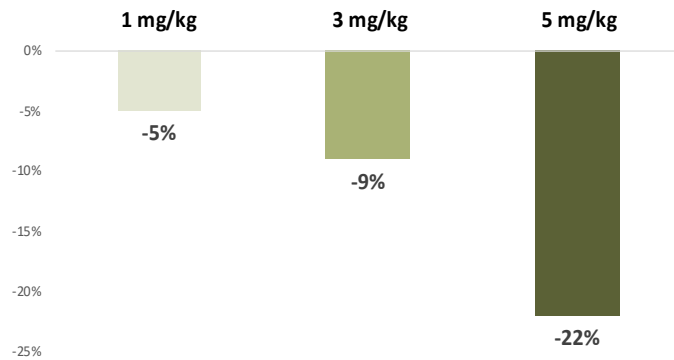
- Oral corticosteroids (OCS) (50-75% of patients)
- Immunosuppressants (30% of patients)
- anti-TNF antibodies (10% of patients)

- No disease modifying therapies available
- Significant toxicity with current treatment options

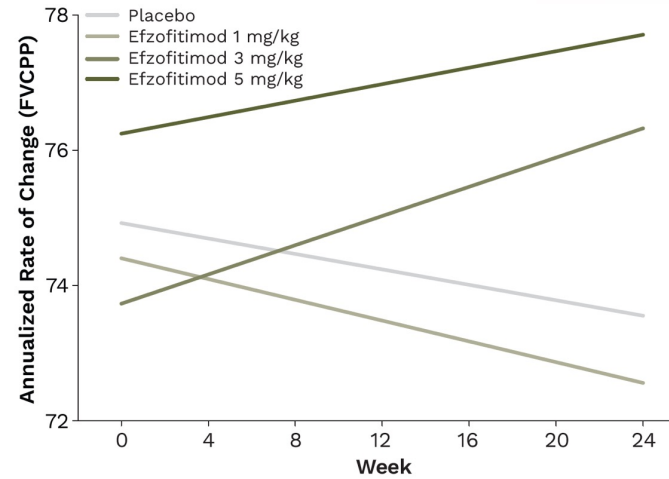
- 1st line as steroid sparing agent
- Avoid current 2nd / 3rd line therapies

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

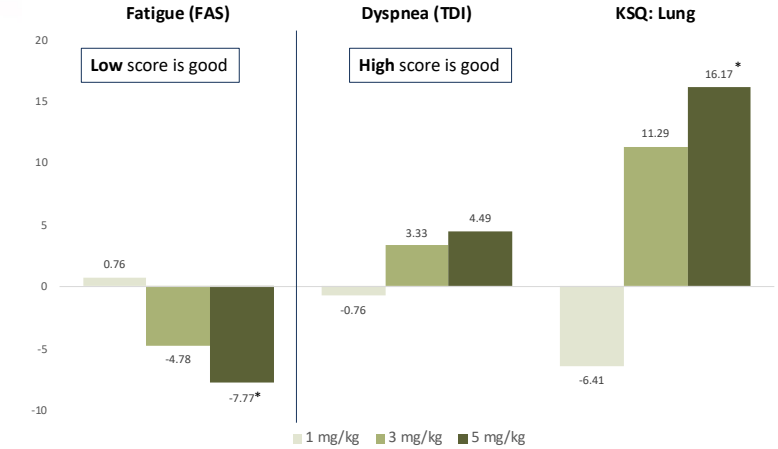
Steroid Sparing



Lung Function



Symptom Control

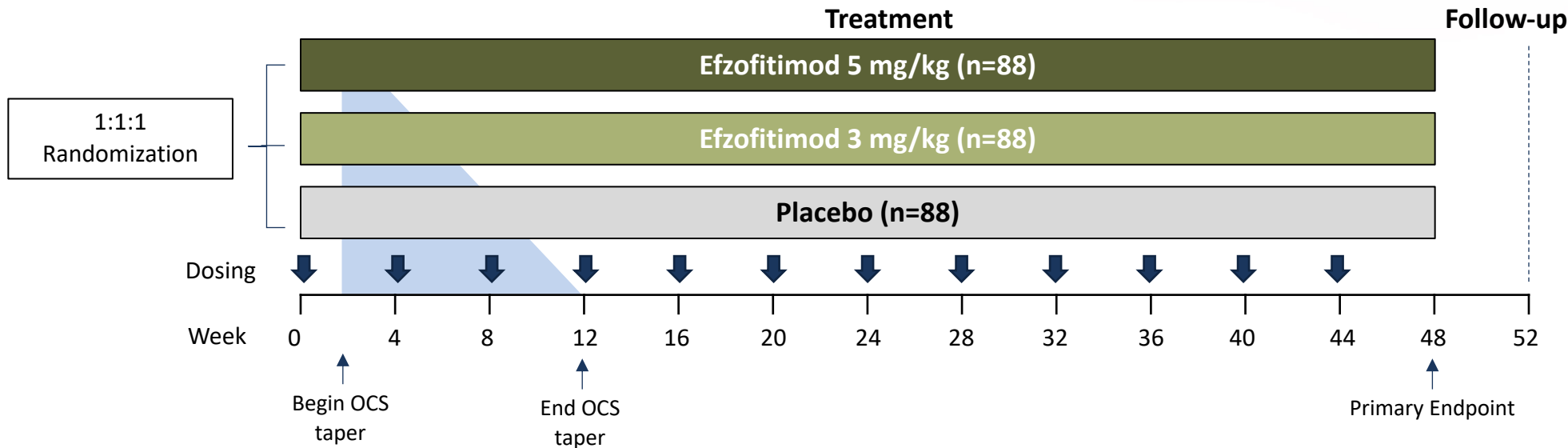


- Primary objective met: Efzofitimid was **safe and well-tolerated** (n=37)
- Secondary objectives met: **Dose-response observed** across all three families of pre-specified endpoints
- Dose-dependent **improvement of inflammatory biomarkers**
- **Robust results:** Pre-specified analysis plan, trends consistent across analysis populations and imputation methods

Global Phase 3 Trial Enrolling in Pulmonary Sarcoidosis



Primary objective: Assess the efficacy of efzofitimid 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 $< 20\%$

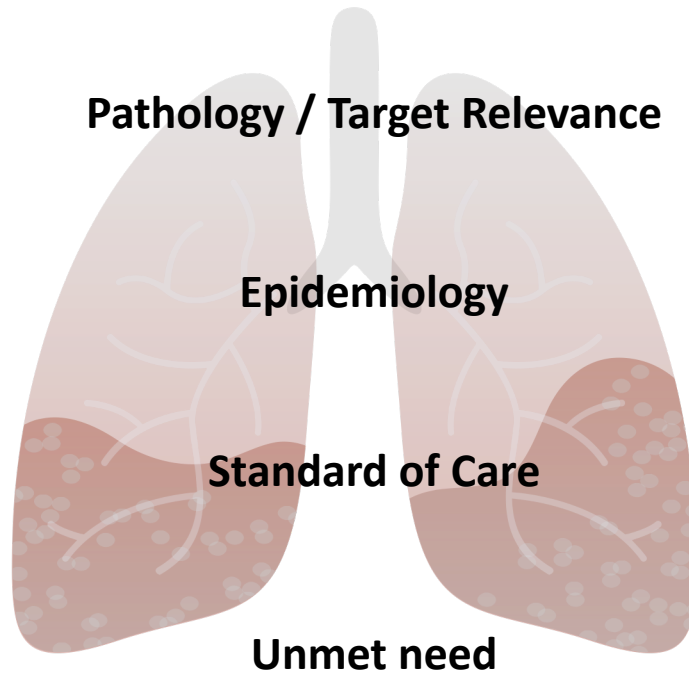
Primary Endpoint

- Steroid burden: change in daily steroid dose

Key Secondary Endpoints

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

SSc-ILD Represents Expanded Commercial Opportunity



Efzofitimod Positioning

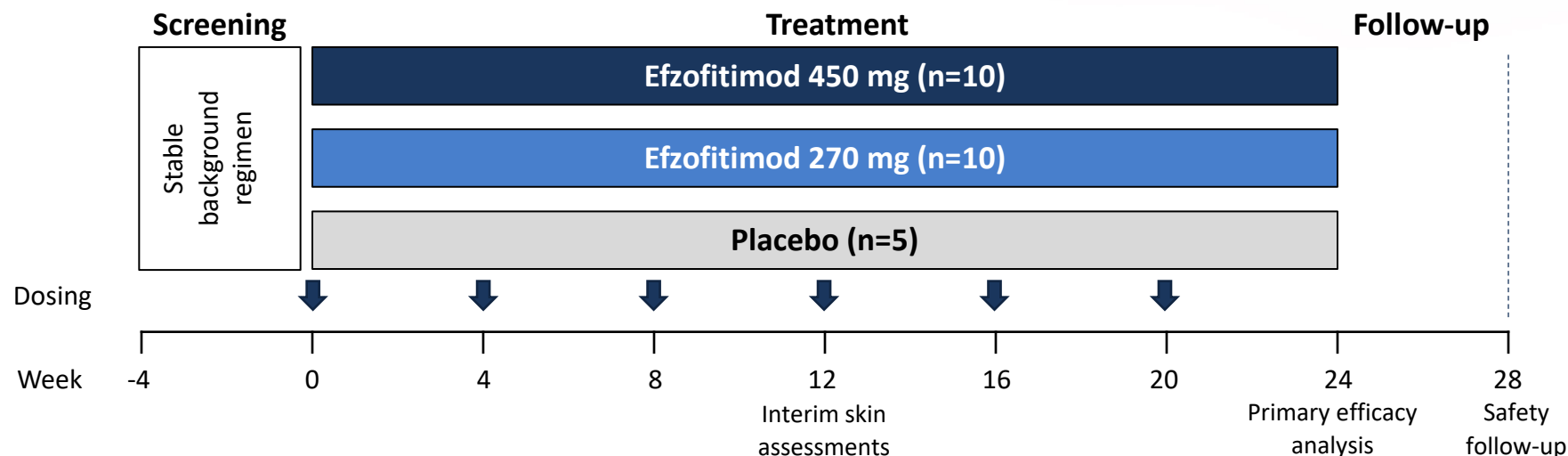
SSc-ILD

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

Phase 2 POC Trial in SSc-ILD Expected to Initiate in Q3 2023



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

Primary Endpoint

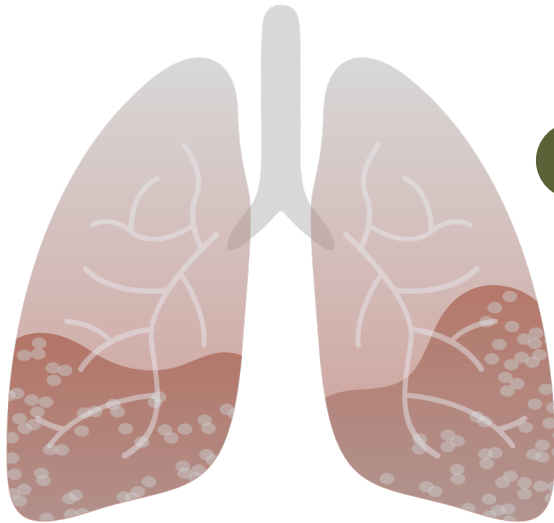
- Lung function: forced vital capacity

Key Secondary Endpoints

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

Efzofitimod Target Value Proposition

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

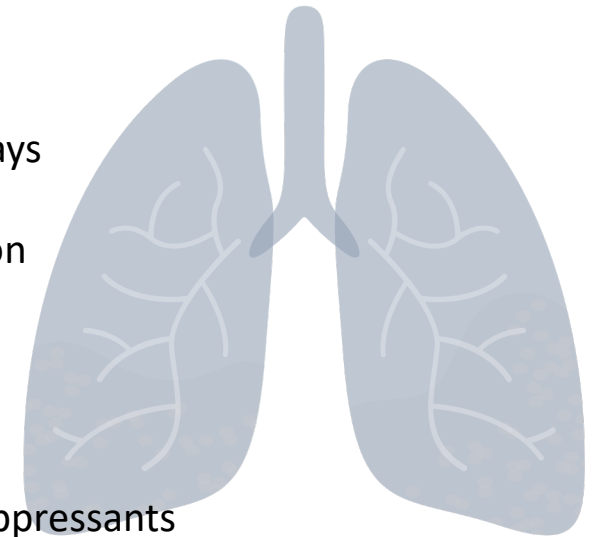


● **Targets innate immunity at site of inflammation**

- 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



*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 enrolling in pulmonary sarcoidosis
- Expansion to second indication with Phase 2 EFZO-CONNECT™ study in SSc-ILD expected to initiate in Q3 2023

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

- ~\$112.0m in cash, restricted cash, cash equivalents and investments as of June 30, 2023
 - Company projects cash runway into 2026
- Partnership for efzofitimid in Japan with Kyorin Pharmaceutical



Thank You