Advancing tRNA synthetase biology

aTyr Pharma

Efzofitimod in Pulmonary Sarcoidosis and Beyond

May 11, 2026

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FDA Type C Meeting Informs Future Efzofitimod Development

Meeting objective: align on the path forward for efzofitimod in pulmonary sarcoidosis

Background

- EFZO-FIT missed its primary endpoint but demonstrated a safety profile consistent with previous trials and durable benefit on multiple clinically meaningful, prespecified quality of life measures
- aTyr was granted a Type C meeting to discuss the EFZO-FIT data, clinical development plan and validation of KSQ-L as a fit-for-purpose endpoint for pulmonary sarcoidosis

Discussion focused on:

- Endpoints (FVC; KSQ-L)
- Our rationale for FVC as endpoint in target patient population
- Dosing (Q3W)
- Safety monitoring
- Benefit / risk profile

Abbreviations: FDA, Food and Drug Administration; KSQ-L, King's Sarcoidosis Questionnaire-Lung; FVC, forced vital capacity

FDA Type C Meeting Informs Future Efzofitimod Development

Meeting outcome: Company to continue development of efzofitimod in pulmonary sarcoidosis incorporating FDA feedback; Company to pursue with new Phase 3 study (C-006)

FDA indicated support for FVC and KSQ-L as clinically meaningful endpoints in pulmonary sarcoidosis

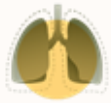
- FDA indicated FVC to be a direct measure of how patients function
- FDA indicated KSQ-L to be a direct measure of how patients feel, and recommended the inclusion of wheezing and cough severity as separate measures of patient symptoms along with new anchors to interpret the clinically meaningful threshold, based on further content validation
- **Our conclusion:** FVC is a more appropriate primary endpoint for C-006, considering FDA has not fully endorsed KSQ-L as fit-for-purpose

FDA reviewed data presenting the rationale for utilizing FVC as an endpoint in the target population for C-006 based on data from EFZO-FIT

Abbreviations: FDA, Food and Drug Administration; KSQ-L, King's Sarcoidosis Questionnaire-Lung; FVC, forced vital capacity

Sarcoidosis has Heterogenous Lung Phenotypes; FVC Relevant Only in Restrictive Phenotype

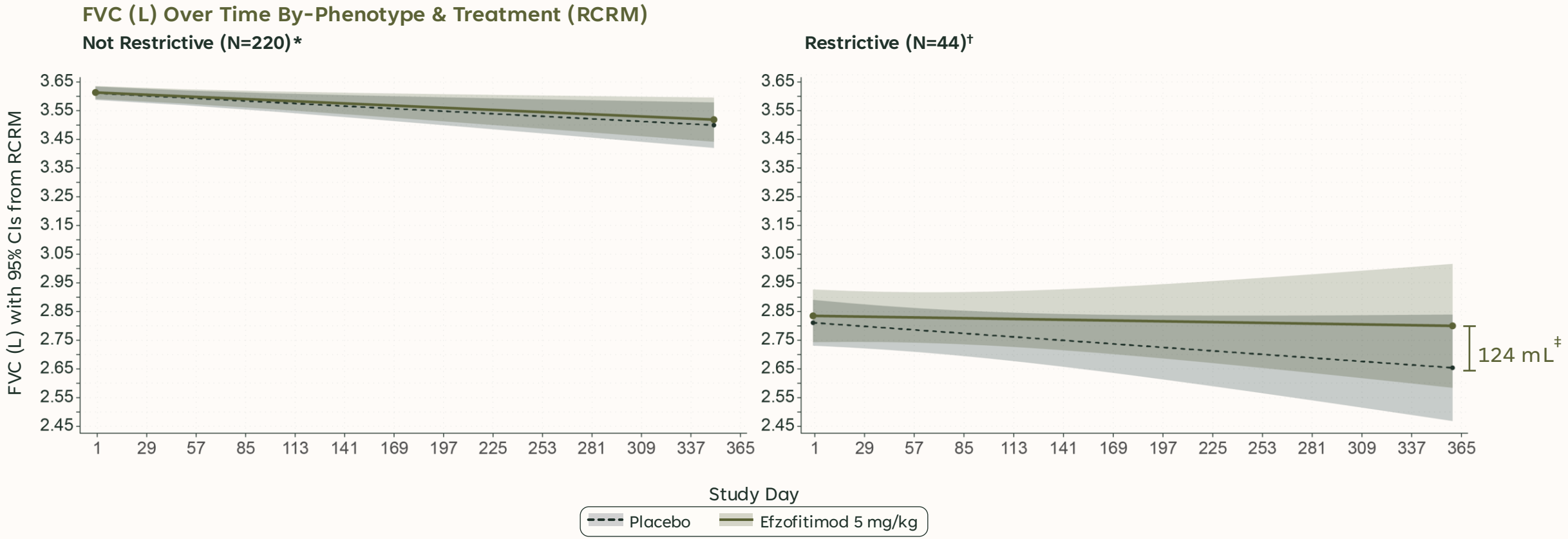
EFZO-FIT enrolled all pulmonary phenotypes; C-006 will create a more homogenous patient population by focusing on one lung phenotype

	Phenotype	Definition*	Sharp, et al* N=562 (%)	EFZO-FIT† N=264 (%)	Relevant Endpoint
	Normal	Not having any impairment	246 (43.8)	89 (33.7)	—
	**Restrictive**	**FVC < lower limit of normal (LLN) with FEV1/FVC ≥ LLN**	**149 (26.5)**	**44 (16.7)**	**FVC**
	Obstructive	FEV1/FVC ≤ LLN with FVC ≥ LLN	71 (12.6)	70 (26.5)	FEV1
	Mixed (combined obstructive/restriction)	FVC < LLN and FEV1/FVC < LLN	50 (8.9)	34 (12.9)	FVC/FEV1
	Isolated diffusion-limited	DLCO < LLN with no restrictive or obstructive defect	46 (8.2)	27 (10.2)	DLCO

*Sharp M, et al. *Ann Am Thorac Soc.* 2023 Jan;20(1):30-37. †Need citation detail. Phenotypes based on z scores, IE criteria will be based on FVCpp and FEV1/FVC ratio and organized hierarchically.
Abbreviations: DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; IE, inclusion/exclusion; LLN, lower limit of normal.

Data from EFZO-FIT Support Our Rationale for FVC as Primary Endpoint in Target Patient Population

Clinically meaningful benefit observed for FVC in patients with restrictive lung disease when treated with efzofitimod



W48 window ends on Study Day 351. *Not Restrictive: includes normal, mixed, obstructive, diffusion limited. †Restrictive: BL FVCpp ≤80% & FEV1/FVC Ratio ≥0.7; ‡RCRM delta between 5mg/kg and placebo at W48.
Abbreviations: Abs, absolute; CDF, cumulative distribution function; CI, confidence interval; FVC, forced vital capacity; L, liter; pp, percent predicted; RCRM, regression coefficient reassessment method; W, week.

FDA Type C Meeting Informs Future Efzofitimod Development

Meeting outcome: Company to continue development of efzofitimod in pulmonary sarcoidosis incorporating FDA feedback; Company to pursue with new Phase 3 study (C-006)

FDA acknowledged reasonableness of the proposed Q3W dosing in the proposed patient population in C-006

- Aligned with FDA on incorporating additional risk mitigation strategies in the protocol
- Safety surveillance for the potential for development of anti-synthetase syndrome will be closely and prospectively monitored
- Data Monitoring Committee will be in place

Benefit / risk profile

- Efzofitimod's benefit / risk profile supports continued development with Q3W dosing in proposed population

Company plans to file IND for C-006 in June 2026

Abbreviations: FDA, Food and Drug Administration; KSQ-L, King's Sarcoidosis Questionnaire-Lung; FVC, forced vital capacity, IND, investigational new drug

Go-Forward Development Plan Leverages Insights from EFZO-FIT and Engagement with FDA

Study design to incorporate key changes intended to demonstrate compelling evidence of efficacy and safety on clinically meaningful endpoint

	EFZO-FIT		New Trial
Primary endpoint	Steroid reduction at week 48	▶	**FVC at week 48**
Study design	All lung phenotypes Forced steroid taper	▶	**Restrictive lung phenotype** **Stable background treatment**
Dosing	5.0 mg/kg Q4W	▶	**5.0 mg/kg Q3W**

Abbreviations: FVC, forced vital capacity; Q3W, every three weeks; Q4W, every four weeks.

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ATYR1923-C-006

A Phase 3 Randomized Double-Blind Placebo-Controlled Study to Evaluate Efzofitimod in Patients with Pulmonary Sarcoidosis

Key endpoints designed to assess how patients function and feel

Target Population: Moderate to severe pulmonary sarcoidosis with restrictive disease

– Enrollment (N≈372)

Primary Endpoint:

– Change from BL in FVC (mL) at W48

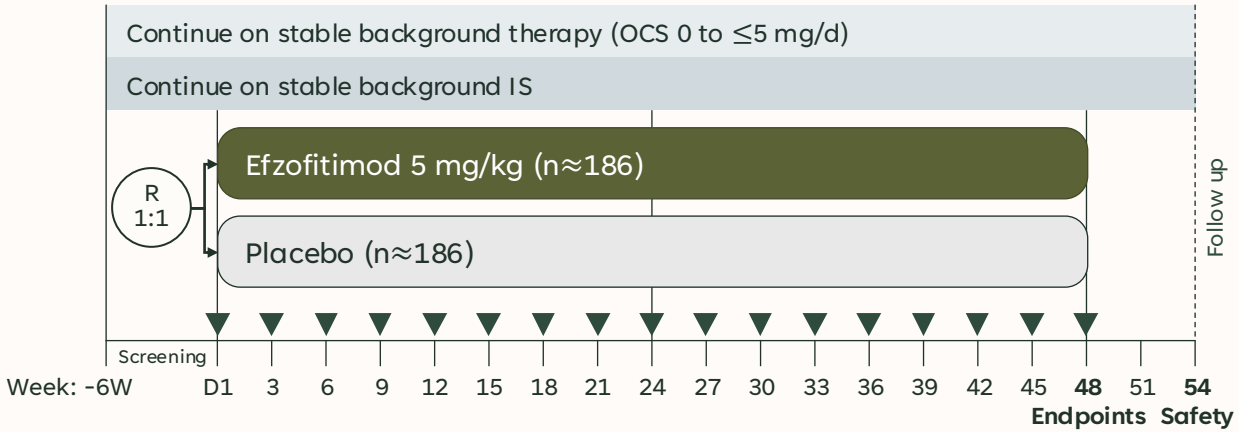
Key Secondary Endpoint:

– Change from BL in KSQ-L score at W48

No steroid taper protocol:

– Participants will remain on stable background therapy of OCS and/or IS

C-006 Study Design



▼ Infusion Q3W for a total of 17 doses

Abbreviations: BL, baseline; D, day; FVC, forced vital capacity; IS, immune suppressant; KSQ-L, King's Sarcoidosis Questionnaire-Lung Score; OCS, oral corticosteroids; Q3W, every three weeks; R, randomized; W, week.

Proposed Key Inclusion and Exclusion Criteria

Study focuses on the right patients for the right endpoints

Inclusion Criteria	Exclusion Criteria
– Documented history of pulmonary sarcoidosis for at least 6 months – Symptomatic pulmonary sarcoidosis: • MRC dyspnea scale grade ≥2 • KSQ-L score ≤60 – Restrictive pulmonary disease: • FVC percent predicted (FVCpp) ≥50% to ≤80% • Forced expiratory volume in 1 second FEV1/FVC ≥0.7 – Stable dose of OCS and/or IS: • OCS dose ≤5 mg/day (prednisone equivalent) for at least 4 weeks • IS treatment for ≥6 months on stable dose for ≥3 months	– HRCT fibrosis score >20% – DLCOpp <40% – Treatment within 4 months with biological immunomodulators, antifibrotics or interleukin inhibitors

Abbreviations: DLCOpp, diffusing capacity of the lungs for carbon monoxide, percent predicted; FEV1, forced expiratory volume in 1 second; FVCpp, forced vital capacity, percent predicted; HRCT, high-resolution computed tomography; IS, immune suppressant; KSQ-L, King's Sarcoidosis Questionnaire-Lung Score; LS, least squares; mMRC, Modified Medical Research Council; OCS, oral corticosteroid.

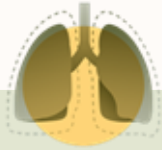
US Pulmonary Sarcoidosis Target Population: ILD Without Advanced Fibrosis

~160k Diagnosed US pulmonary sarcoidosis patients†

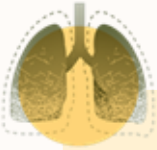
~90k Moderate to severe disease
(Symptomatic, functional impairment, with or without fibrosis)

~18k
Obstructive

~24k
Mixed / Diffusion-limited



~38k
Restrictive*



~10k
Advanced fibrosis†

Efzofitimod Target Population

- 38k–62k patients in US alone
- Patients with restrictive lung disease without advanced fibrosis
- Upside opportunity in mixed/diffusion-limited patients

*<80% FVCpp; FEV1/FVC ≥0.7. †>20% on HRCT; †Diagnosed pulmonary means ICD10 code D86.0 or D86.2.
Sharp M, et al. *Ann Am Thorac Soc.* 2023 Jan;20(1):30-37; Obi O, et al. *Chest.* 2024 Apr; 165(4):892-907.
Abbreviations: FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; pp, percent predicted.

Thank You

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