Advancing tRNA synthetase biology

aTyr Pharma

Efzofitimod in Pulmonary Sarcoidosis and Beyond

October 2026

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aTyr's Strategic Outlook: Creating First-In-Class Therapies that Modulate New Pathways in Inflammatory and Fibrotic Diseases

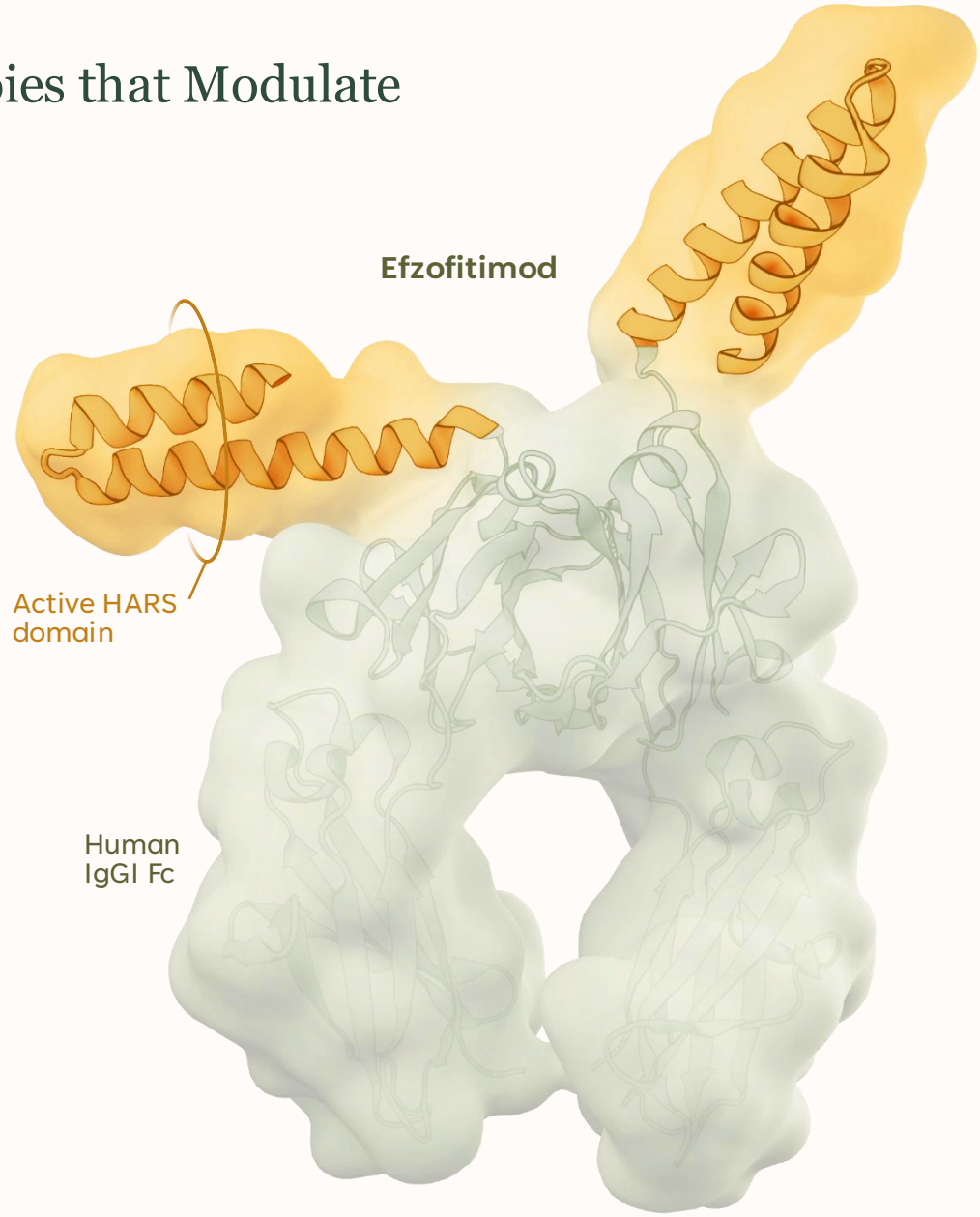
aTyr is advancing a platform based on tRNA synthetase biology to build a pipeline focused on inflammation and fibrosis

Efzofitimod is a biologic immunomodulator with a novel complementary mechanism of action:

- **EFZO-FIT:** largest interventional pulmonary sarcoidosis trial conducted to date; generated key insights being used to optimize the path forward for efzofitimod
- **Planned Phase 3 study in pulmonary sarcoidosis** refines primary endpoint, study design, and dosing
- **EFZO-CONNECT:** advancing efzofitimod in Phase 2 SSc-ILD study
- Efzofitimod for ILD represents up to a $5B market opportunity[1]

Lead preclinical candidate ATYR0101 in development for fibrosis is currently undergoing IND-enabling studies

aTyr retains a robust IP-protected tRNA synthetase library



[1]aTyr Pharma, Inc. data on file.
Abbreviations: ILD, interstitial lung disease; IP, intellectual property; SSc-ILD, systemic sclerosis-associated interstitial lung disease; tRNA, transfer ribonucleic acid.

Sarcoidosis is a Serious Orphan Disease in Desperate Need of a Safe and Effective FDA-Approved Treatment



Disease pathology

- Inflammatory disease that can affect any organ
- 90% of cases affect the lungs (pulmonary sarcoidosis)
- Characterized by noncaseating granulomas resulting from an immunologic cascade driven by proinflammatory macrophages
- Overexpression of neuropilin-2 (NRP2) in sarcoid granulomas



Epidemiology

- Orphan disease with more than 1M patients worldwide; 160k in the US[1]
- More common in women
- 3X as common in people of African descent
- >50% of patients experience moderate-severe disease with organ impairment
- 1 in 5 progress to fibrosis



Unmet Need

- Severely impaired QoL with debilitating symptoms including cough, dyspnea and fatigue
- Risk of progression and organ failure
- Increased risk of hospitalization and mortality
- Limited SoC: steroids, cytotoxic IST and TNF inhibitors have poor clinical evidence and substantial toxicity



Commercial Opportunity

- Large diagnosed rare disease population
- No FDA-approved therapy in 70+ years
- Disease and treatment burden cause psychological and socioeconomic impact
- Underserved market without near-term competition

[1]aTyr Pharma, Inc. data on file.
Abbreviations: IST, immunosuppressive therapy; QoL, quality of life; SoC, standard of care, TNF, tumor necrosis factor.

A New Candidate for Pulmonary Sarcoidosis

A biologic immunomodulator that targets NRP2 on activated macrophage cells to resolve inflammation without immune suppression and may prevent fibrosis progression

Targets new immune receptor to restore immune balance:

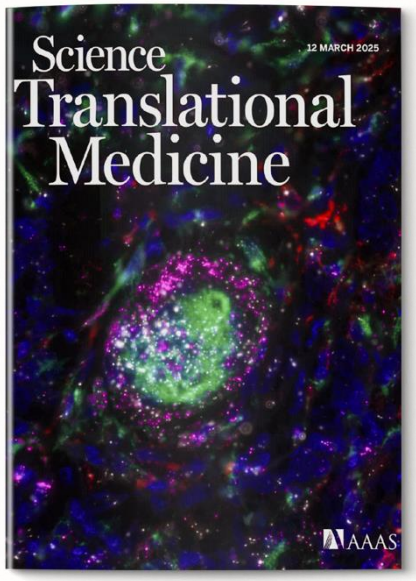
- Selectively modulates NRP2
- Downregulates multiple pro-inflammatory pathways
- Broad anti-inflammatory effect without immune suppression

Preclinical data:

- Demonstrated anti-inflammatory and anti-fibrotic effects in multiple models of lung inflammation and fibrosis

Phase 1b/2a trial in pulmonary sarcoidosis:[1]

- Efzofitimod was safe and well-tolerated
- Dose-response observed across three families of pre-specified endpoints compared to placebo: lung function; quality of life; steroid reduction



Cover photo shows NRP2 expression in sarcoid granuloma[2]


SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

INTERSTITIAL LUNG DISEASE

A human histidyl-tRNA synthetase splice variant therapeutic targets NRP2 to resolve lung inflammation and fibrosis

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

[1]Culver D, et al., *CHEST*. 2023;163, 881-890. [2]Nangle LA, et al. *Sci Transl Med*. 2025 Mar 12;17(789):eadp4754. Abbreviations: NRP2, neuropilin-2.

EFZO-FIT: Largest Interventional Trial Conducted in Pulmonary Sarcoidosis

Target Population: Moderate to severe pulmonary sarcoidosis

- Enrollment: N=268[1]
- Dx of pulmonary sarcoidosis for ≥6 mos
- Stable treatment with ≥7.5 and ≤25 mg/d OCS
- Extent of fibrosis <20%
- Symptomatic with KSQ-L score ≤70

Primary Endpoint:*

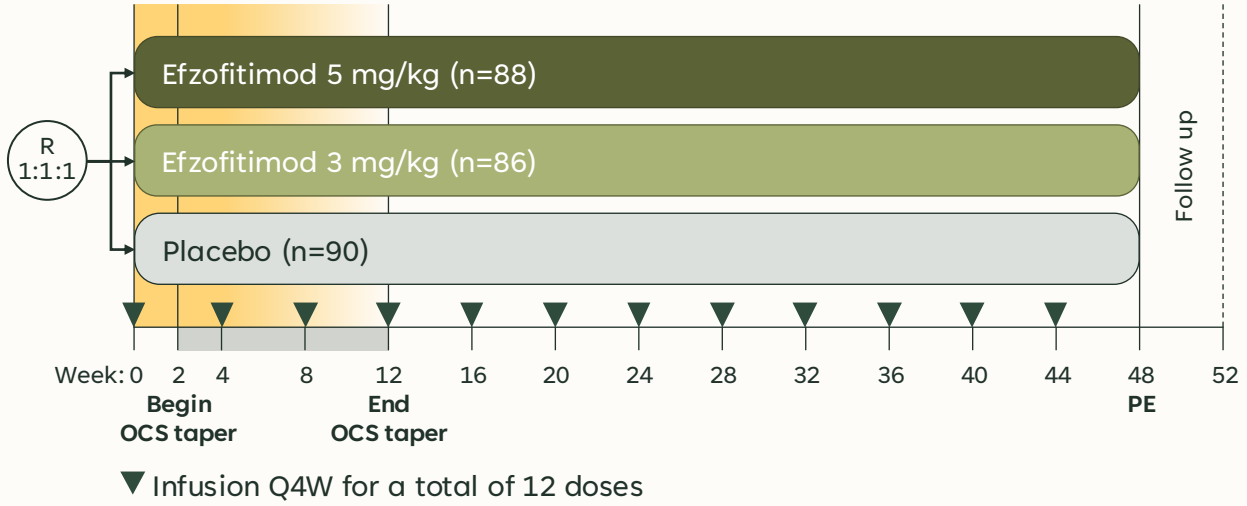
- Change from BL in mean daily OCS dose at W48

Protocol-guided steroid taper

Global trial conducted at 85 centers in 9 countries:

- Many trial sites are WASOG centers of excellence

EFZO-FIT Study Design



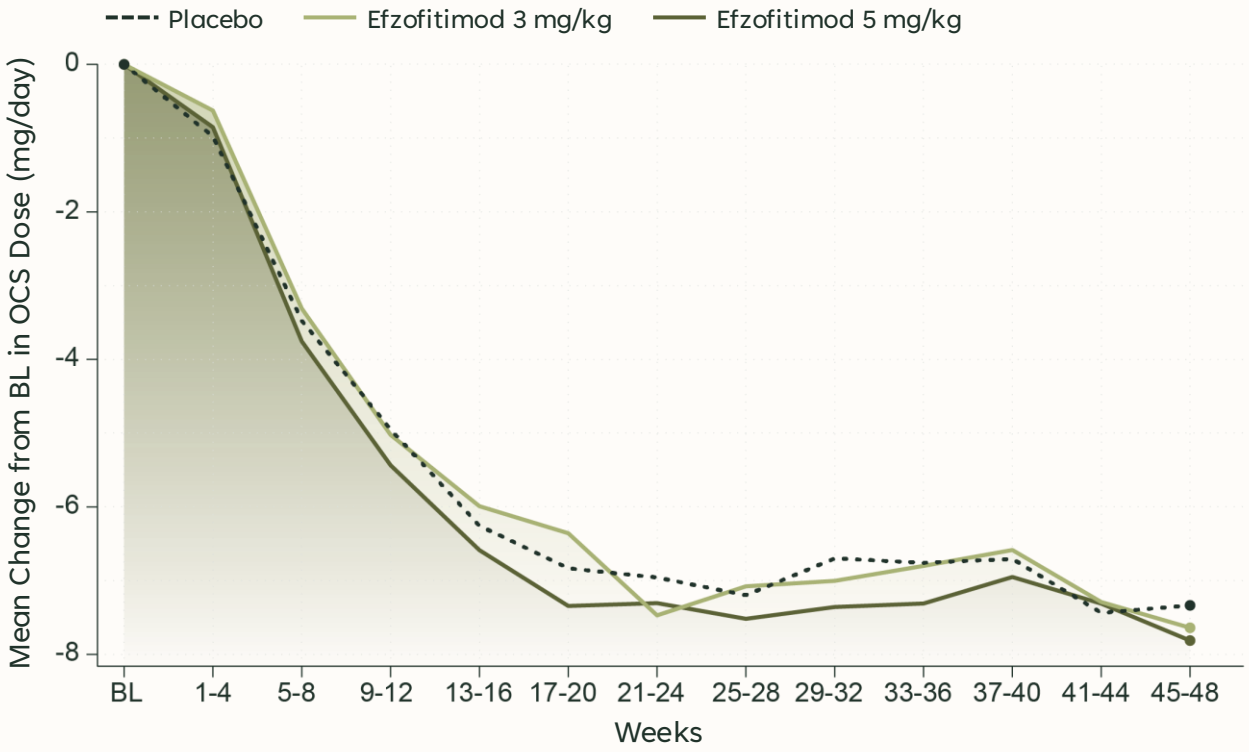
[1]268 patients were randomized; 264 patients were randomized and dosed
Topline data reported Q3 '25. *Time frame BL to W48.
Abbreviations: BL, baseline; Dx, diagnosis; KSQ-L, King's Sarcoidosis Questionnaire-Lung Score; OCS, oral corticosteroids; PE, primary endpoint; Q4W, every four weeks; R, randomized; W, week; WASOG, World Association for Sarcoidosis and Other Granulomatous Disorders.

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Substantial Steroid Reduction Observed in all EFZO-FIT Groups Provides Important Insights

Although the primary endpoint of the study was not met, we learned that patients with chronic, symptomatic pulmonary sarcoidosis can be managed for prolonged periods on lower doses of OCS without worsening of disease

ITT: Mean Change from BL in OCS Dose Over Time (Primary Endpoint)



Steroid Free at Week 48

	Placebo N=90	Efzofitimod 3 mg/kg N=86	Efzofitimod 5 mg/kg N=88
Steroid free; n (%)	36 (40.2)	45 (51.8)	46 (52.6
Odds ratio (95% CI)	—	1.6 (0.9, 3.0)	1.7 (0.9, 3.1)
p-value	—	*0.1172*	*0.0919*

Note: The study's statistical analysis plan was designed on a hierarchical assessment basis. As the primary endpoint did not achieve statistical significance, p-values for other endpoints are reported and should be interpreted as nominal p-values.
Abbreviations: BL, baseline; CI, confidence interval; ITT, intention to treat; OCS, oral corticosteroids; W, week.

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Evidence of Clinical Activity Demonstrated Across Multiple Pre-specified QoL Endpoints

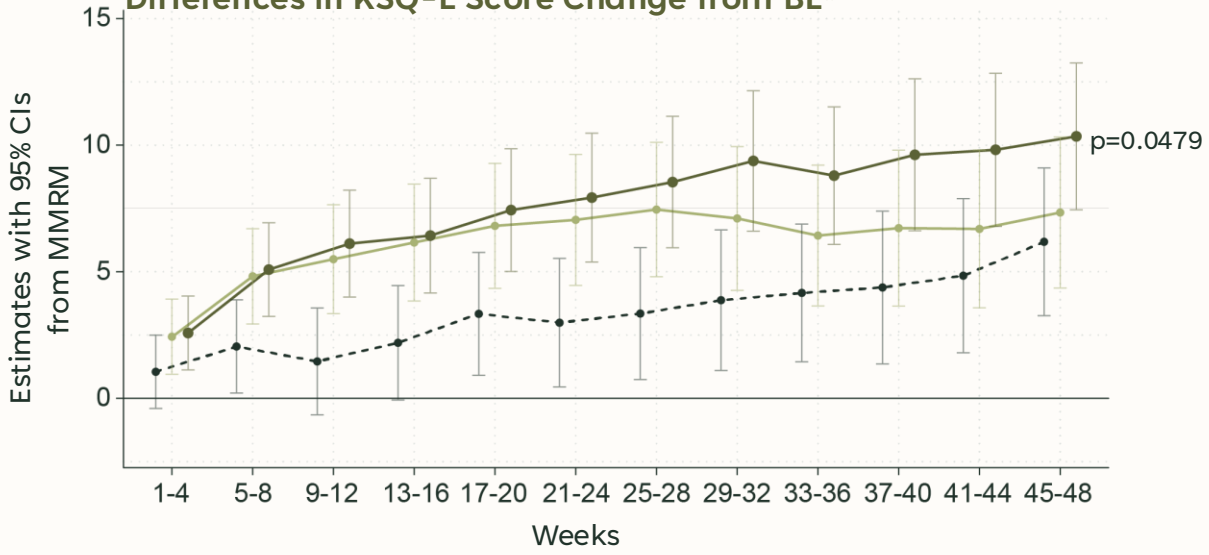
KSQ-L measures how much pulmonary sarcoidosis affects a patient's perceived respiratory QoL:

- By weeks 9-12, KSQ-L was significantly increased in patients on 5.0 mg/kg efzofitimod relative to placebo
- Increased KSQ-L represents improved QoL

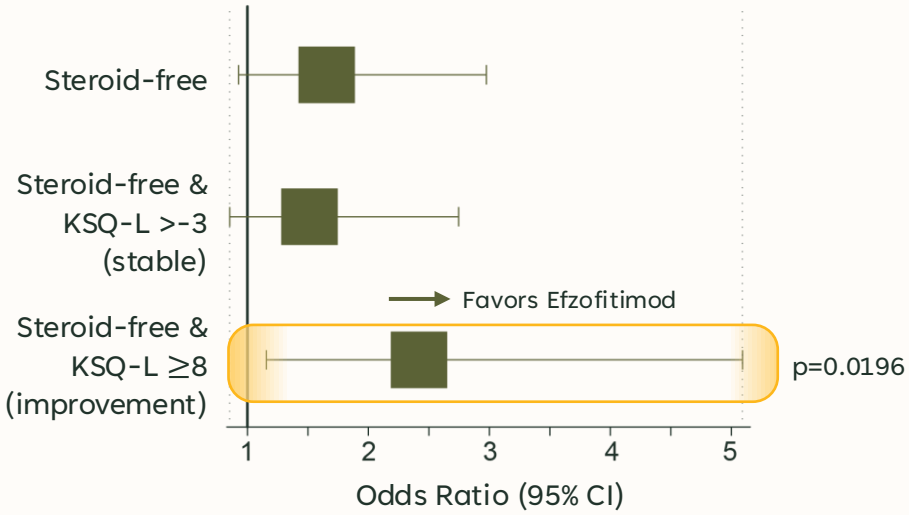
Steroid reduction and KSQ-L composite endpoint measures whether patients could both reduce steroids and improve QoL:

- More patients met the composite of steroid-free with improved KSQ-L on 5.0 mg/kg efzofitimod

Differences in KSQ-L Score Change from BL*



Efzofitimod 5 mg/kg vs Placebo from Logistic Regression



Placebo | Efzofitimod 3 mg/kg | Efzofitimod 5 mg/kg

*Difference in LS Means from Placebo (with 95% CIs) from MMRM. Abbreviations: BL, baseline; CI, confidence interval; KSQ-L, King's Sarcoidosis Questionnaire-Lung Score; LS, least squares; MMRM, mixed model for repeated measures; QoL, quality of life.

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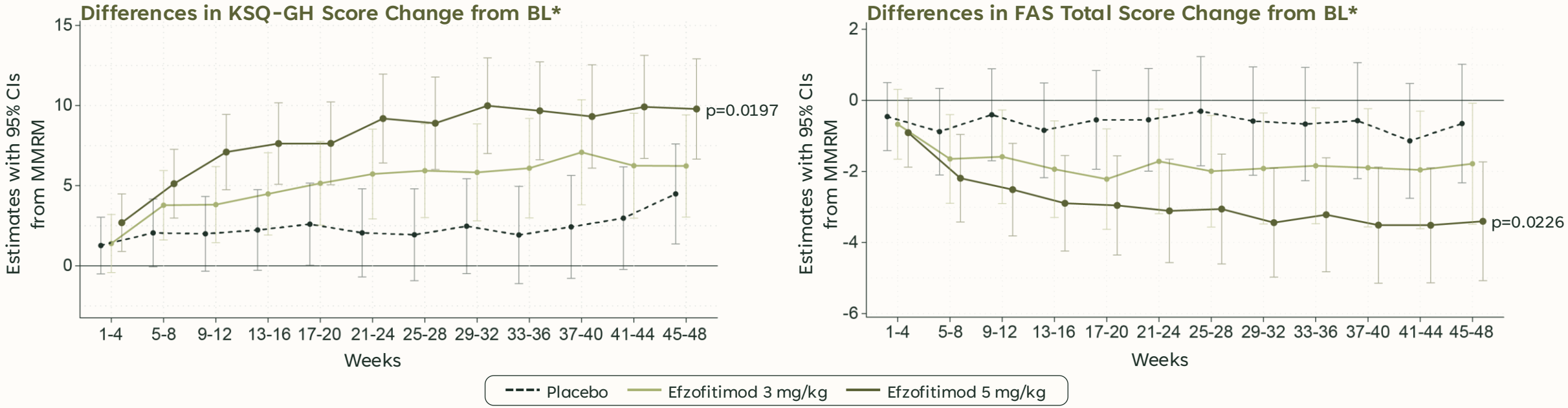
Evidence of Clinical Activity Demonstrated Across Multiple Pre-specified QoL Endpoints

KSQ-GH measures how much pulmonary sarcoidosis affects a patient's perceived general health:

- By weeks 9-12, KSQ-GH was significantly increased in patients on 5.0 mg/kg efzofitimod relative to placebo
- Increased KSQ-GH represents improved QoL

FAS measures how much fatigue affects the patient:

- By weeks 9-12, FAS was significantly decreased in patients on 5.0 mg/kg efzofitimod relative to placebo
- Decreased FAS represents improved fatigue



*Difference in LS Means from Placebo (with 95% CIs) from MMRM. Abbreviations: BL, baseline; CI, confidence interval; FAS, fatigue assessment scale; KSQ-GH, King's Sarcoidosis Questionnaire-General Health Score; LS, least squares; MMRM, mixed model for repeated measures; QoL, quality of life.

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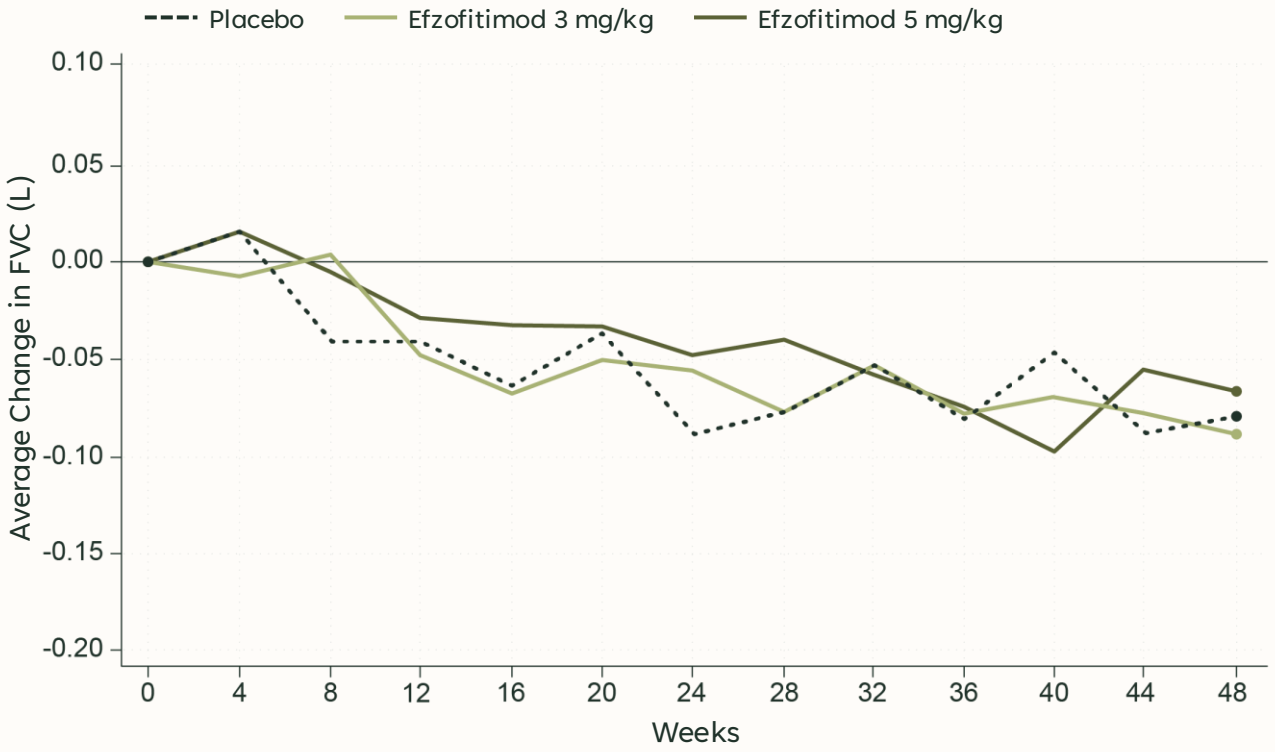
Forced Vital Capacity Maintained Despite Steroid Taper

EFZO-FIT enrolled a heterogenous patient population with various pulmonary phenotypes

FVC at Week 48 (MMRM)

	Placebo N=90	Efzofitimod 3 mg/kg N=86	Efzofitimod 5 mg/kg N=88
LS means at W48 (mL)	3380.4	3369.7	3395.4
LS means change from BL (mL)	-84.5	-95.1	-69.4
Difference in LS mean (mL) (95% CI)	—	-10.6 (-104.7, 83.5)	15.1 (-77.4, 107.6)
p-value	—	*0.8244*	*0.7485*

Change from BL in FVC (L) Over Time



*Difference in LS Means from Placebo (with 95% CIs) from MMRM.
Abbreviations: BL, baseline; CI, confidence interval; FVC, forced vital capacity; L, liter; LS, least squares; MMRM, mixed model for repeated measures; W, week.

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Efzofitimod was Generally Well-Tolerated with Consistent Safety Profile

- Efzofitimod was generally well-tolerated at both the 3.0 mg/kg and 5.0 mg/kg doses, consistent with a previously observed safety profile in all trials conducted to date
- AEs were mostly mild or moderate in severity and generally assessed as unrelated to the study drug
- SAEs were limited and balanced between groups
- Proportion of patients with treatment-related SAEs and events leading to discontinuation was small and balanced between groups
- Proportion of patients who developed antidrug antibodies was small and balanced between groups

Abbreviations: AE, adverse event; SAE, serious adverse event.

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FDA Type C Meeting Informs Future Efzofitimod Development

Objective: align on the path forward for efzofitimod in pulmonary sarcoidosis
Outcome: Company to continue development of efzofitimod in pulmonary sarcoidosis incorporating FDA feedback and alignment on protocol for new Phase 3 study (C-006)

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

- KSQ-L: FDA 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

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 reached alignment with FDA on protocol for C-006 in September 2026 and plans to initiate study-related activities in Q4 2026

Abbreviations: FDA, Food and Drug Administration; FVC, forced vital capacity; IND, investigational new drug; KSQ-L, King's Sarcoidosis Questionnaire-Lung; Q3W, every three weeks.

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

FVC has been used as a registrational endpoint in related ILD indications, with approvals being granted for placebo adjusted differences as low as 45 mL

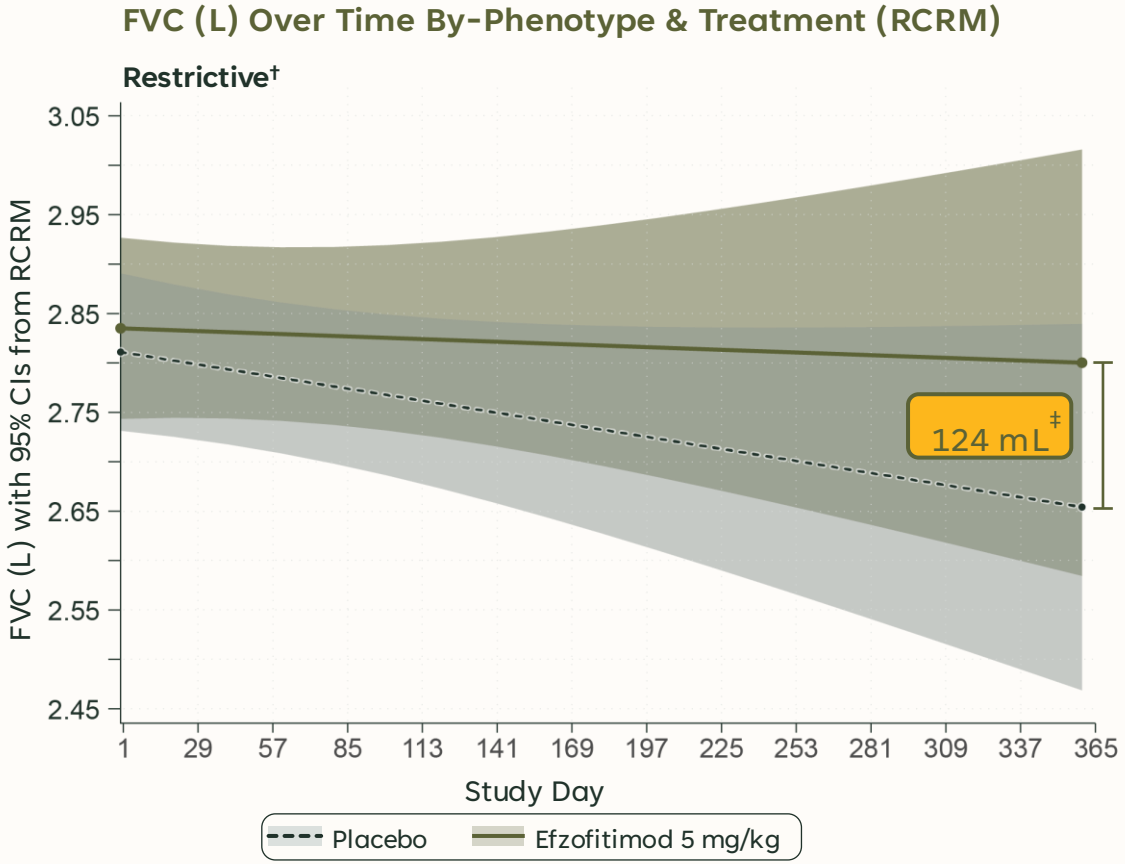
	Phenotype	Definition*	Real-World Data* N=562 (%)	EFZO-FIT† N=264 (%)	Relevant Endpoint
	Normal	Not having any impairment	246 (43.8)	89 (33.7)	—
	**Restrictive**	**FVC < lower limit of normal (LLN) with FEV1/FVC ≥ LLN**	**149 (26.5)**	**44 (16.7)**	**FVC**
	Obstructive	FEV1/FVC ≤ LLN with FVC ≥ LLN	71 (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. †Data on file.
Abbreviations: DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limit of normal.

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

Clinically meaningful FVC benefit observed at week 48 in patients with restrictive lung disease when treated with efzofitimod



Baseline characteristics were generally similar to the ITT population with a few notable exceptions

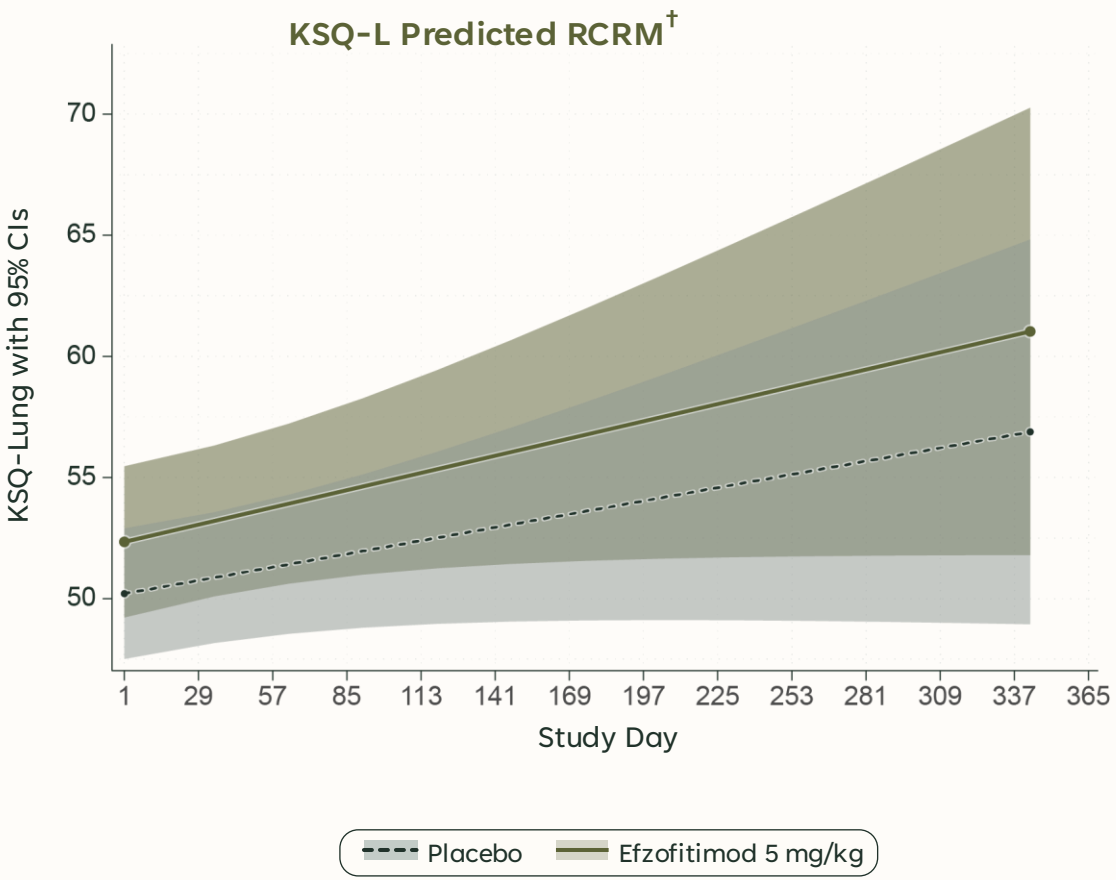
- Expectedly, the FVCpp in the restrictive subset (~70%) was lower when compared to the ITT population (~88%)
- AE profile was generally similar to the ITT population with the exception that wheezing was not reported in the restrictive subset

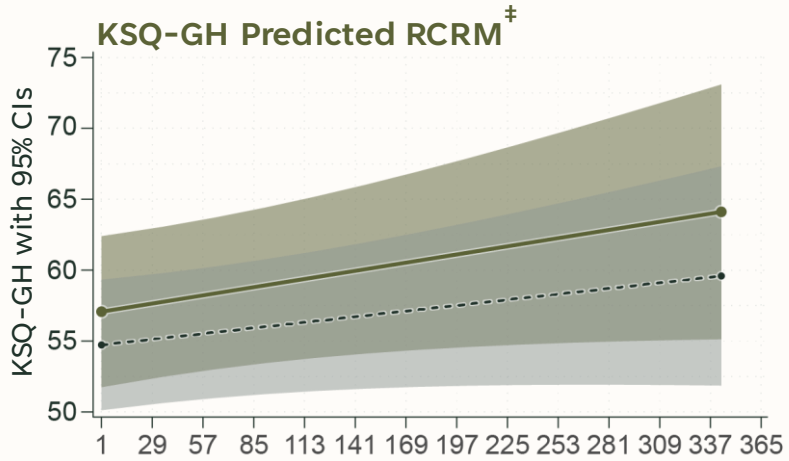
Efzofitimod 5 mg/kg showed trends toward greater steroid reduction vs placebo in the restrictive population

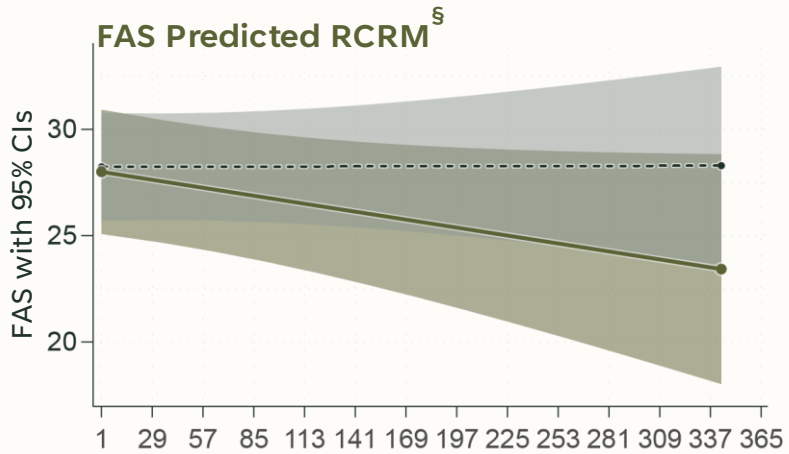
- OCS reduction from baseline observed at W48: 74% vs 58%
- Steroid free observed at W48: 50% vs 40%
- Relapse (steroid rescue for >14d) observed at W48: 8% vs 31%

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: CI, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FVCpp, forced vital capacity, percent predicted; ITT, intention-to-treat; L, liter; OCS, oral corticosteroids; RCRM, regression coefficient reassessment method; W, week.

Benefit on PROs Observed in EFZO-FIT in ITT Remains Consistent in Restrictive* Population







*Restrictive by FVCpp: Baseline FVCpp ≤80% & FEV1/FVC ration ≥0.7. †RCRM model est. adj. for Baseline MMLUNGSS. ‡RCRM model est. adj. for Baseline MMGENHSS. §RCRM model est. adj. for Baseline MMFASTOT. Week 48 window ends on Study Day 351. Abbreviations: CI, confidence interval; FAS, Fatigue Assessment Scale; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FVCpp, forced vital capacity, percent predicted; ITT, intention-to-treat; KSQ-GH, King's Sarcoidosis Questionnaire-General Health; KSQ-L, King's Sarcoidosis Questionnaire-Lung; MMLUNGSS, baseline lung symptom score; MMFASTOT, baseline fatigue total score; MMGENHSS, baseline general health score; PRO, patient-reported outcome; RCRM, repeated continuous reassessment method.

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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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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

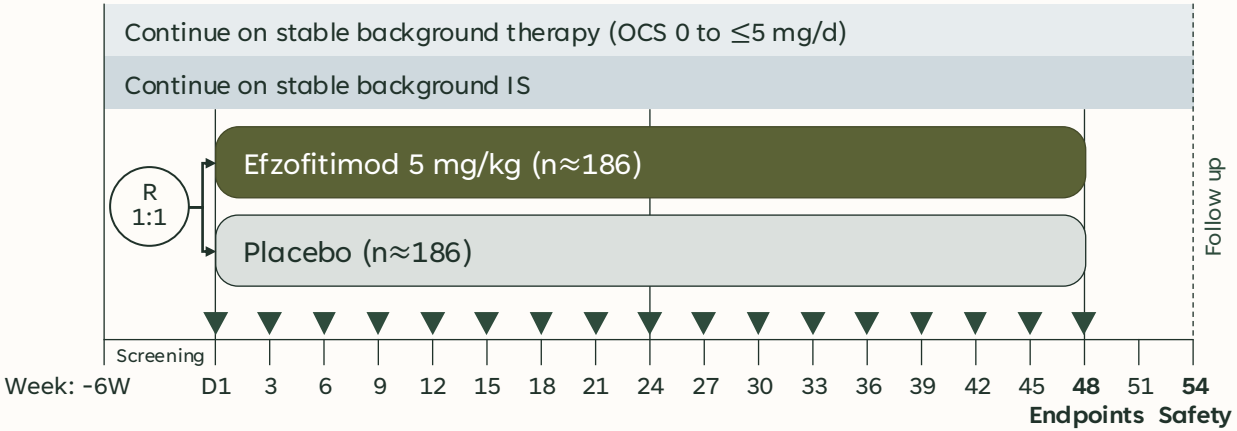
Key Secondary Endpoint:

– 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.

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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; MRC, Modified Medical Research Council; OCS, oral corticosteroid.

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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

- Patients with restrictive lung disease without advanced fibrosis
- Upside opportunity in mixed and/or diffusion-limited patients
- Up to 62k patients in US alone

*<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; FVCpp, forced vital capacity, percent predicted; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; pp, percent predicted.

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Efzofitimod Targets NRP2 Biology to Reset Pro-Inflammatory Macrophages

Disease State

1. Immune triggers recruit pro-inflammatory macrophages.

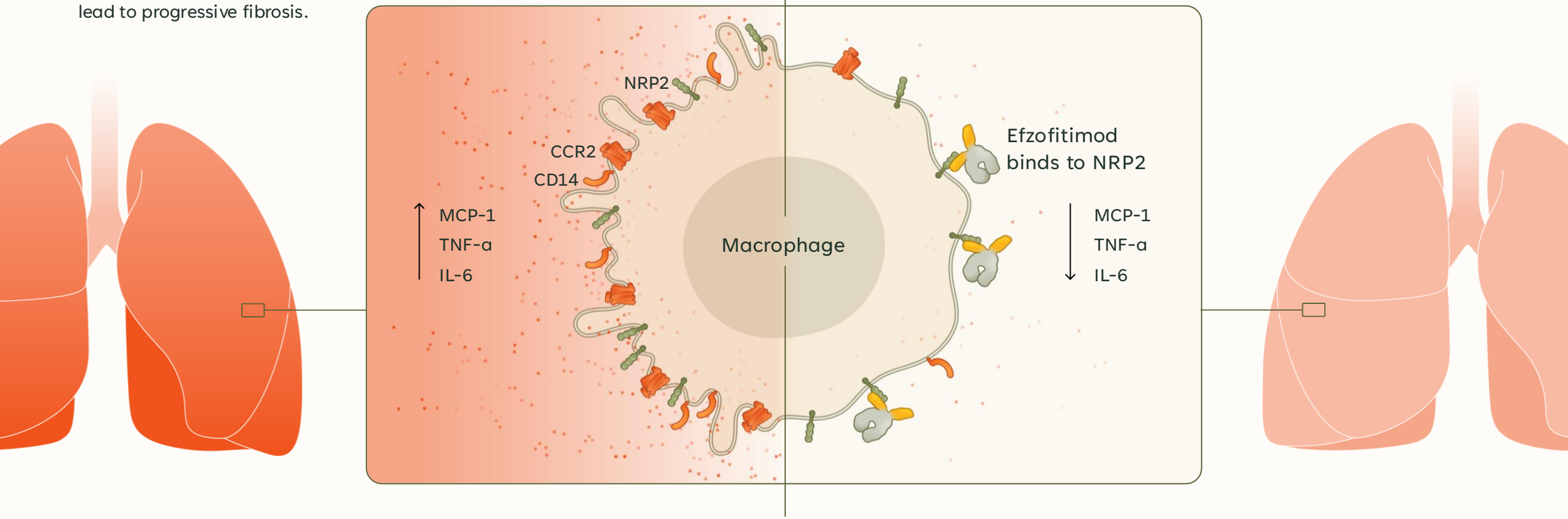
   Persistent inflammation can lead to progressive fibrosis.

2. Pro-inflammatory macrophages express inflammatory factors, as well as NRP2, a regulator of inflammatory state.

Efzofitimod MOA

3. Efzofitimod binds to NRP2, promoting a less inflammatory macrophage population.

4. Key drivers of inflammation and fibrosis are downregulated.



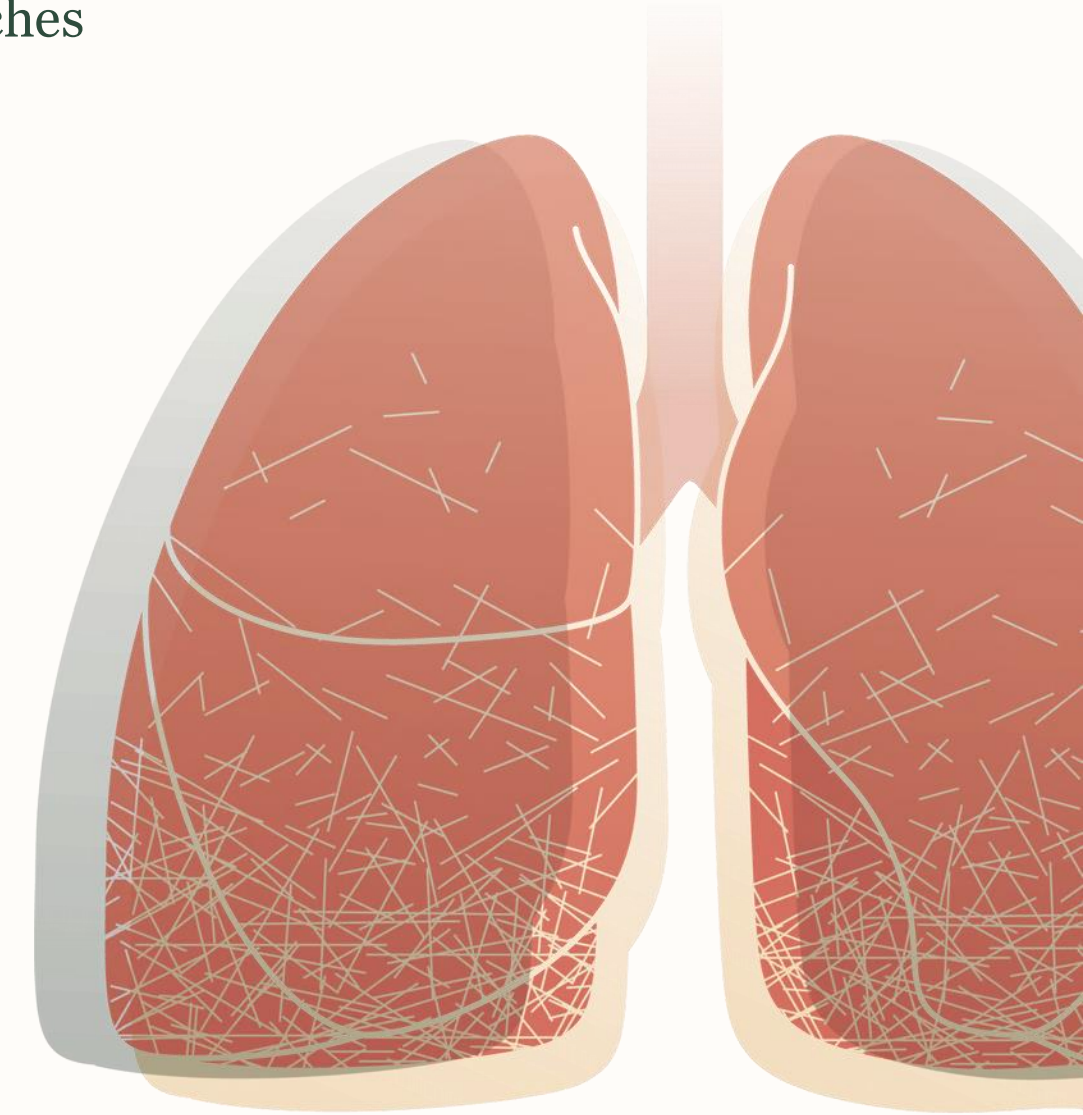
Nangle LA, et al. *Sci Transl Med.* 2025 Mar 12;17(789):eadp4754.
Abbreviations: CCR2, C-C Chemokine Receptor Type 2; CD14, cluster of differentiation 14; IL-6, interleukin-6; MCP-1, monocyte chemoattractant protein-1; MOA, mechanism of action; NRP2, neuropilin-2; TNF-α, tumor necrosis factor-alpha.

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Interstitial Lung Disease Requires New Treatment Approaches

Efzofitimod's novel and complementary MOA may address the significant unmet medical need in ILD

- ILD is an umbrella term including >200 rare lung disorders characterized by inflammation and scarring of the lung interstitium
- Many ILDs share common clinical presentations and pathologic features, and are managed similarly to pulmonary sarcoidosis with immunomodulatory therapy
- Treatment goals are to improve QoL and prevent permanent lung damage caused by fibrosis
- Current therapies are toxic, slow disease decline at best, and do not improve QoL
- Most drug development efforts have focused on the fibrotic side of the ILD market (IPF/PPF), leaving the larger inflammatory side of the market untapped and in need of innovation
- Up to $5B market opportunity[1]



[1]aTyr Pharma, Inc. data on file.
Abbreviations: ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; MOA, mechanism of action; PPF, progressive pulmonary fibrosis; QoL, quality of life.

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SSc-ILD is a Common and Deadly Manifestation of Systemic Sclerosis



Disease pathology

- Chronic, progressive autoimmune disease
- Characterized by inflammation and fibrosis of the skin and other organs, including the lungs
- >50% of patients experience ILD
- Key immune mediators include IL-6, MCP-1 and BAL neutrophil infiltration



Epidemiology

- More than 1.5M patients worldwide with SSc-ILD; ~60k in the US
- Average age of onset between 45-55
- 70-90% of ILD develops within first 3 years of SSc diagnosis
- 30% of patients develop fibrosis



Unmet Need

- Debilitating disease manifestations impacting QoL with high morbidity and mortality
- 3X greater mortality risk than SSc alone
- Limited treatment options with only 2 approved therapies
- Current therapies only slow decline with no QoL benefit

Abbreviations: BAL, bronchoalveolar lavage; IL-6, interleukin-6; ILD, interstitial lung disease; MCP-1, monocyte chemoattractant protein-1; SSc, systemic sclerosis; SSc-ILD, systemic sclerosis-associated interstitial lung disease; QoL, quality of life.

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Phase 2 Study to Evaluate the Efficacy, Safety, and Tolerability of Efzofitimod in Patients with SSc-ILD

Enrollment completed; topline results expected in Q1 2027

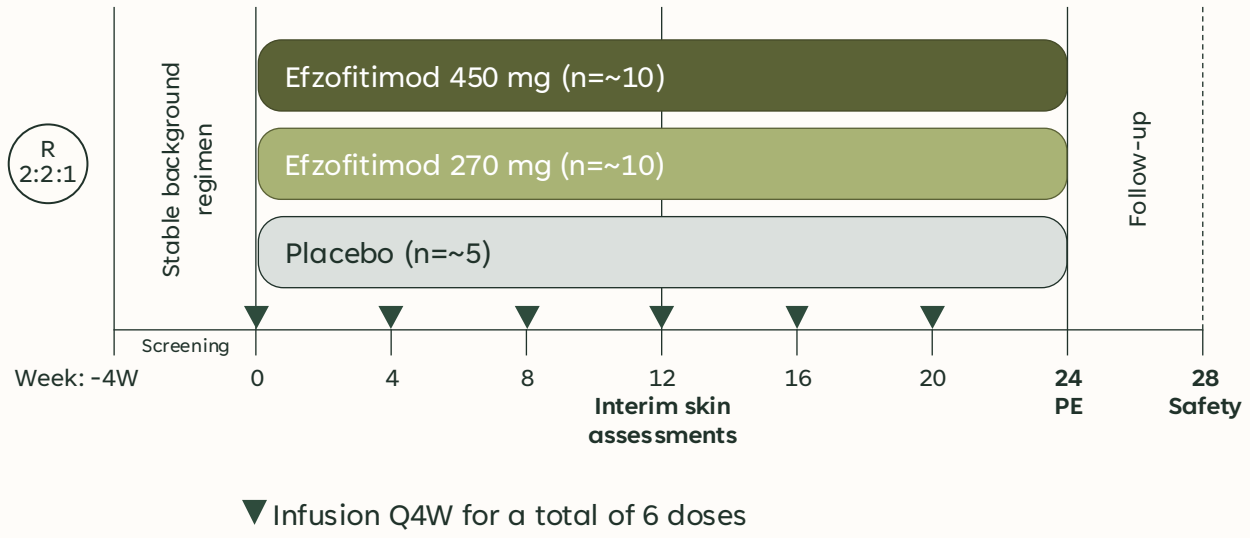
Target Population: SSc with progressive ILD
- Enrollment: N=23
- Patients with SSc (ACR/EULAR criteria), and ILD (BL HRCT)
- Progressive disease (recent onset, evidence for inflammation, diffuse cutaneous SSc)
- On background mycophenolate therapy or equivalent

Primary Objective:
- Assess the efficacy of efzofitimod on pulmonary, cutaneous, and systemic manifestations in SSc-ILD

Primary Endpoint:
- Lung function: FVC

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

EFZO-CONNECT Study Design



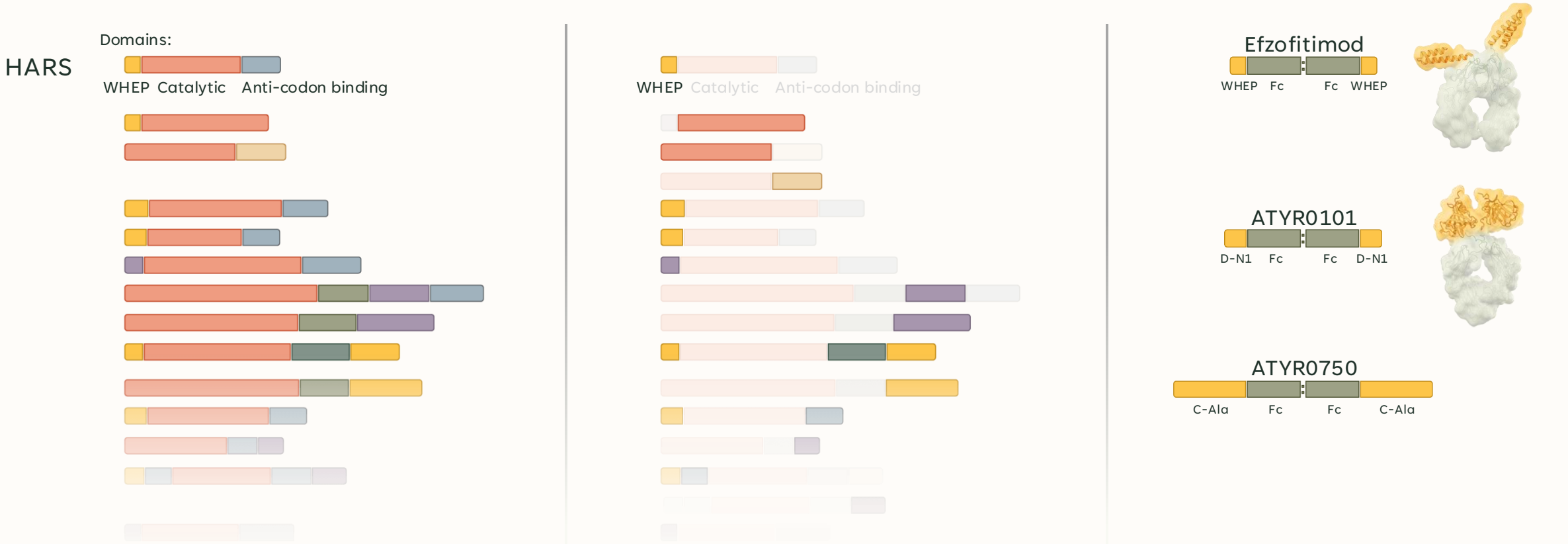
Abbreviations: ACR, American College of Rheumatology; BL, baseline; EULAR, European League Against Rheumatism; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; PE, primary endpoint; PRO, patient reported outcome; mRSS, modified Rodnan Skin Score; Q4W, every 4 weeks; SSc, systemic sclerosis; SSc-ILD, systemic sclerosis-associated interstitial lung disease; W, week.

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Our tRNA Synthetase Library: Potential Candidates in a New Class of Medicine

Full-length tRNA synthetases → **Natural fragments and variants** → **Pipeline products**

Novel extracellular functions gained through evolutionary intelligence



Abbreviations: C-Ala, C-terminal alanine-binding domain; D-N1, N-terminal domain 1; Fc, fragment crystallizable region (of an antibody); HARS, histidyl-tRNA synthetase; tRNA, transfer ribonucleic acid; WHEP, domain named after the proteins in which it was first identified: tryptophanyl-tRNA synthetase (W), histidyl-tRNA synthetase (H), and glutamyl-prolyl-tRNA synthetase (EP).

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Efzofitimod Leads a Growing Pipeline of tRNA Synthetase-Derived Biologics

PROGRAM	tRNA SYNTHETASE	MOA	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Efzofitimod	HARS	NRP2 modulator	Pulmonary Sarcoidosis				
			SSc-ILD	efzo-connect			
			Other ILD				
ATYR0101	DARS	Myofibroblast depleter	Fibrosis				
ATYR0750	AARS	FGFR4 modulator	Fibrosis				
tRNA Synthetase Candidates[1]	Multiple	Multiple	Multiple				

[1]Pipeline candidates in development based on additional tRNA synthetases from IP portfolio.
Abbreviations: AARS, alanyl-tRNA synthetase; DARS, aspartyl-tRNA synthetase; FGFR4, fibroblast growth factor receptor 4; HARS, histidyl-tRNA synthetase; ILD, interstitial lung disease; IP, intellectual property; MOA, mechanism of action; NRP2, neuropilin-2; SSc-ILD, systemic sclerosis-associated interstitial lung disease; tRNA, transfer ribonucleic acid.

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aTyr's Strategic Outlook

Advancing a platform based on tRNA synthetase biology to build a pipeline focused on inflammation and fibrosis

Pulmonary sarcoidosis	Efzofitimod opportunity	Pipeline, IP and cash
Efzofitimod is a biologic immunomodulator with a novel and complementary mechanism of action	Efzofitimod in position to be first to market in pulmonary sarcoidosis without near term competition	aTyr retains a robust IP-protected tRNA synthetase library
EFZO-FIT: largest interventional pulmonary sarcoidosis trial conducted to date generated key insights being used to optimize the path forward for efzofitimod	Therapeutic potential beyond sarcoidosis - advancing efzofitimod in SSc-ILD	Advancing additional pre-clinical candidates for fibrosis
Planned Phase 3 study in pulmonary sarcoidosis refines primary endpoint, study design, and dosing	Efzofitimod for ILD represents up to a $5B market opportunity[1]	~$58.9M in cash, restricted cash, cash equivalents and available-for-sale investments as of June 30, 2026; cash runway into late 2028 based on current operations[2]

[1]aTyr Pharma, Inc. data on file. [2]Future development of efzofitimod in the planned Phase 3 study in pulmonary sarcoidosis will require aTyr to obtain additional capital through equity or debt financings, grant funding, collaborations, strategic partnerships and/or licensing arrangements.
Abbreviations: ILD, interstitial lung disease; IP, intellectual property; SSc-ILD, systemic sclerosis-associated interstitial lung disease; tRNA, transfer ribonucleic acid.

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Appendix

EFZO-FIT: Subgroup Analysis in Restrictive Population

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Restrictive Population: Baseline Characteristics Generally Similar to ITT Population

Baseline characteristics were generally similar to the ITT population with a few notable exceptions

- Expectedly the FVC in the restrictive subset (FVC pp ~ 70%) was lower when compared to the ITT population (~ 88%)
- The mean weight in the restrictive subset (~ 88 to 95 kilos) was higher when compared to the ITT population (~ 85 kilos)
- Likewise, the mean BMI in the restrictive subset (~ 30 kg/m2) was higher when compared to the ITT population (~ 29 kg/m2)

Baseline characteristics between treatment groups in the restrictive subset

- There were non-substantive imbalances between treatment groups

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Restrictive Population: Baseline Demography

Weight was overall higher in the restrictive subset than the ITT. Obesity can contribute to a restrictive phenotype.

	Placebo (N=16)	3 mg/kg (N=16)	5 mg/kg (N=12)
Gender – Female, n (%)	6 (37.5)	7 (43.8)	5 (41.7)
Race – Black, n (%)	5 (31.2)	3 (18.8)	3 (25)
Weight in kg, mean (sd)	88.9 (19.1)	86.6 (24.4)	95.9 (20.3)
BMI in kg/m^2, mean (sd)	30.2 (4.5)	29 (5.4)	32.4 (8.8)
Age in years, mean (sd)	52.4 (10.9)	54.6 (12.3)	57.8 (8.1)

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Restrictive Population: Baseline Disease Characteristics

	Placebo (N=16)	3 mg/kg (N=16)	5 mg/kg (N=12)
Disease duration in years, mean (sd)	9.78 (9.44)	10.13 (9.37)	4.17 (4.21)
Baseline OCS in mg/day, mean (sd)	10.88 (4.7)	11.72 (3.38)	11.88 (4.54)
OCS duration, n (%)			
0 to <2 years	8 (50)	10 (62.5)	5 (41.7)
≥2 years	8 (50)	6 (37.5)	7 (58.3)
Concomitant Immunosuppressant, n (%)	9 (56.3)	7 (43.8)	6 (50)
Baseline KSQ-L, mean (sd)	46.69 (12.73)	49.7 (7.01)	48.26 (10.01)
Baseline MRC dyspnea score, mean (sd)	1.75 (0.58)	1.69 (0.70)	1.58 (0.67)

Baseline OCS dose, OCS duration, phenotype (obstructive/mixed) and immunosuppressant use are covariates in the MMRM

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Restrictive Population: Extrapulmonary Involvement

Less extrapulmonary Involvement in Efzofitimod 5 mg/kg group

Extra Pulmonary Involvement Ongoing (At Screening)	Placebo N = 16 n (%)	3 mg/kg N = 16 n (%)	5 mg/kg N = 12 n (%)
Any extra pulmonary involvement	6 (37.5)	5 (31.3)	1 (8.3)
Extrapulmonary lymph nodes	3 (18.8)	2 (12.5)	0
Cutaneous	1 (6.3)	1 (6.3)	0
Bone and Joint	0	1 (6.3)	0
Hepatic	1 (6.3)	0	1 (8.3)
Ophthalmic	2 (12.5)	1 (6.3)	0
Other	0	0	1 (8.3)
Cardiac	0	1 (6.3)	0

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Restrictive Population: MRC Dyspnea Score

MRC dyspnea score	Placebo N = 16 n (%)	3 mg/kg N = 16 n (%)	5 mg/kg N = 12 n (%)
Grade 0	0	0	0
Grade 1	5 (31.2)	7 (43.8)	6 (50)
Grade 2	10 (62.5)	7 (43.8)	5 (41.7)
Grade 3	1 (6.2)	2 (12.5)	1 (8.3)
Grade 4	0	0	0

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Restrictive Population: Baseline Pulmonary Characteristics

Lower baseline FVC for restrictive patients compared to ITT.

	Placebo (N=16)	3 mg/kg (N=16)	5 mg/kg (N=12)
FVC in Liters			
N	16	16	12
Mean (SD)	2.851 (0.839)	2.710 (0.819)	2.795 (0.467)
Range	1.467 – 4.093	1.169 – 4.436	2.043 – 3.544
FVC pp in %			
N	16	16	12
Mean (SD)	70.82 (8.78)	68.48 (7.24)	71.32 (4.29)
Range	50.08 – 79.91	52.99 – 79.95	64.13 – 77.19
FEV1 in Liters			
N	16	16	12
Mean (SD)	2.234 (0.660)	2.156 (0.673)	2.257 (0.423)
Range	1.157 – 3.203	0.904 – 3.710	1.717 – 3.071
FEV1 pp in %			
N	16	16	12
Mean (SD)	69.33 (8.63)	68.46 (8.64)	73.01 (6.62)
Range	48.41 – 79.34	52.34 – 83.24	64.81 – 83.30

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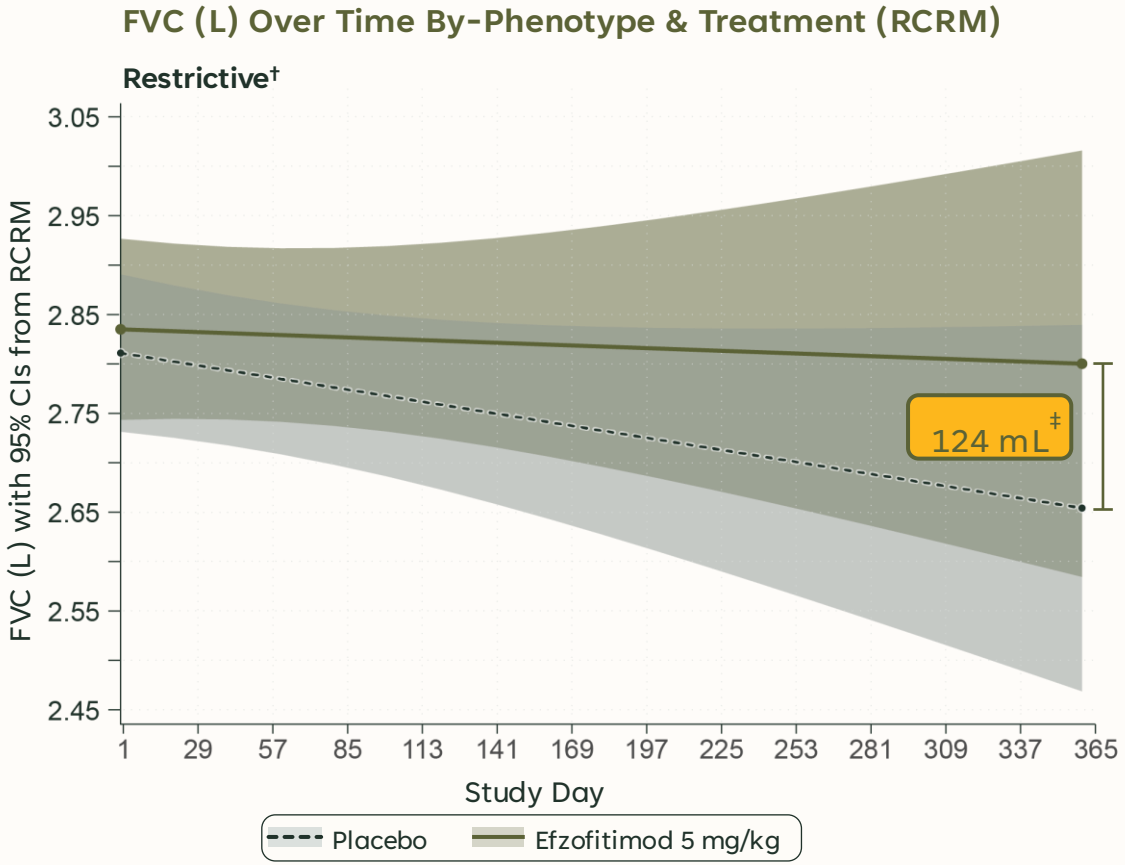
Restrictive Population: Baseline Pulmonary Characteristics

	Placebo (N=16)	3 mg/kg (N=16)	5 mg/kg (N=12)
DLco in mL/min/mmHg			
N	13	16	12
Mean (SD)	17.08 (5.33)	16.88 (6.90)	18.42 (6.63)
Range	6.12, 26.17	7.54, 28.27	10.26, 32.30
DLco pp 2017 in %			
N	13	16	12
Mean (SD)	67.72 (16.75)	65.79 (19.49)	73.93 (25.04)
Range	31.48, 95.86	40.45, 111.17	46.56, 133.60

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Restrictive Population: FVC Data Support Our Rationale for FVC as Primary Endpoint in Target Patient Population for Study C-006

Clinically meaningful FVC benefit observed at week 48 in patients with restrictive lung disease when treated with efzofitimod



Baseline characteristics were generally similar to the ITT population with a few notable exceptions

- Expectedly, the FVCpp in the restrictive subset (~70%) was lower when compared to the ITT population (~88%)
- AE profile was generally similar to the ITT population with the exception that wheezing was not reported in the restrictive subset

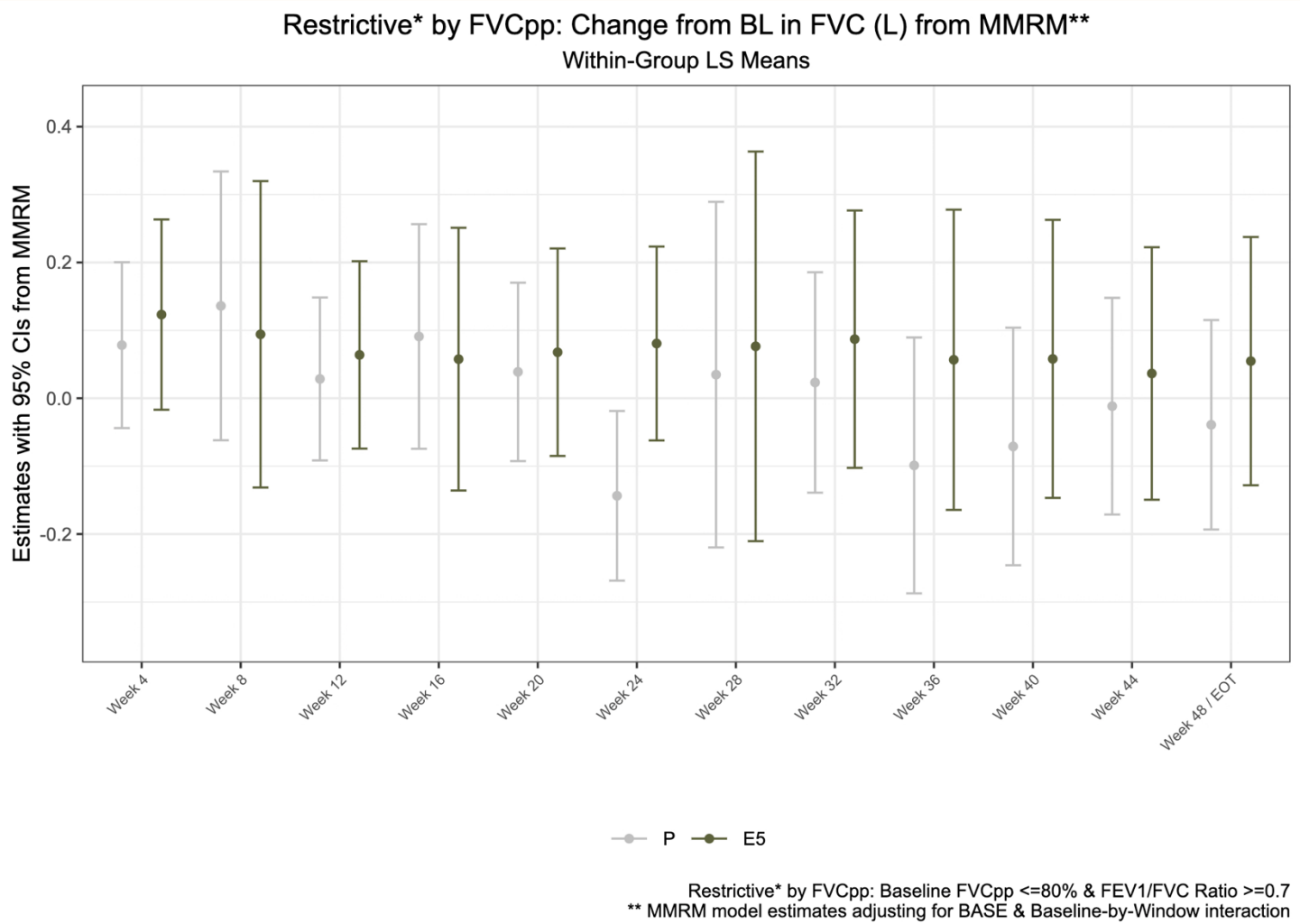
Efzofitimod 5 mg/kg showed trends toward greater steroid reduction vs placebo in the restrictive population

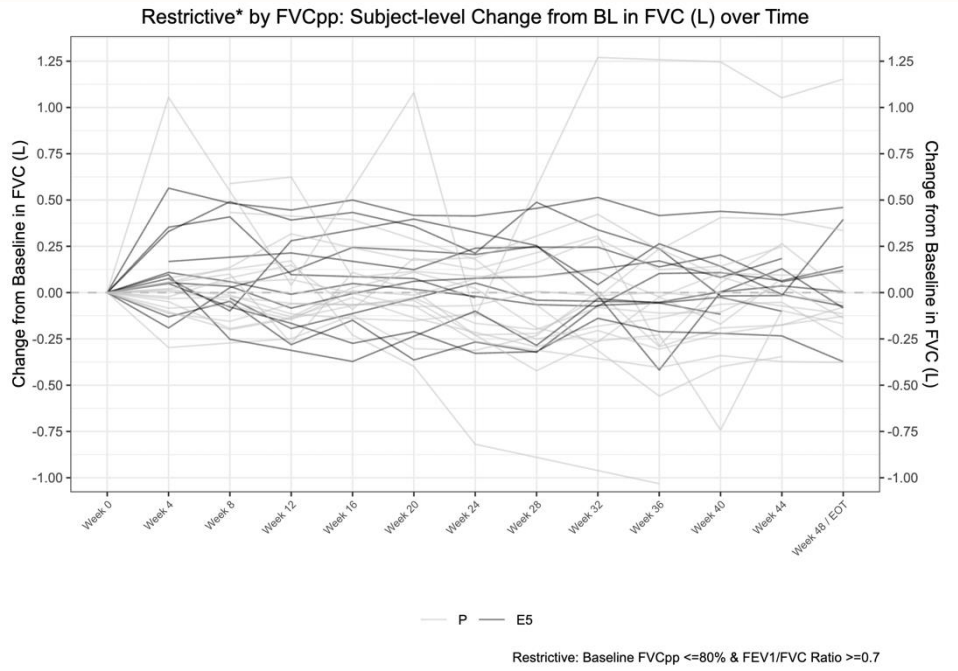
- OCS reduction from baseline observed at W48: 74% vs 58%
- Steroid free observed at W48: 50% vs 40%
- Relapse (steroid rescue for >14d) observed at W48: 8% vs 31%

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: CI, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FVCpp, forced vital capacity, percent predicted; ITT, intention-to-treat; L, liter; OCS, oral corticosteroids; RCRM, regression coefficient reassessment method; W, week.

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Restrictive Population: FVC (L) MMRM Change from Baseline to Week 48



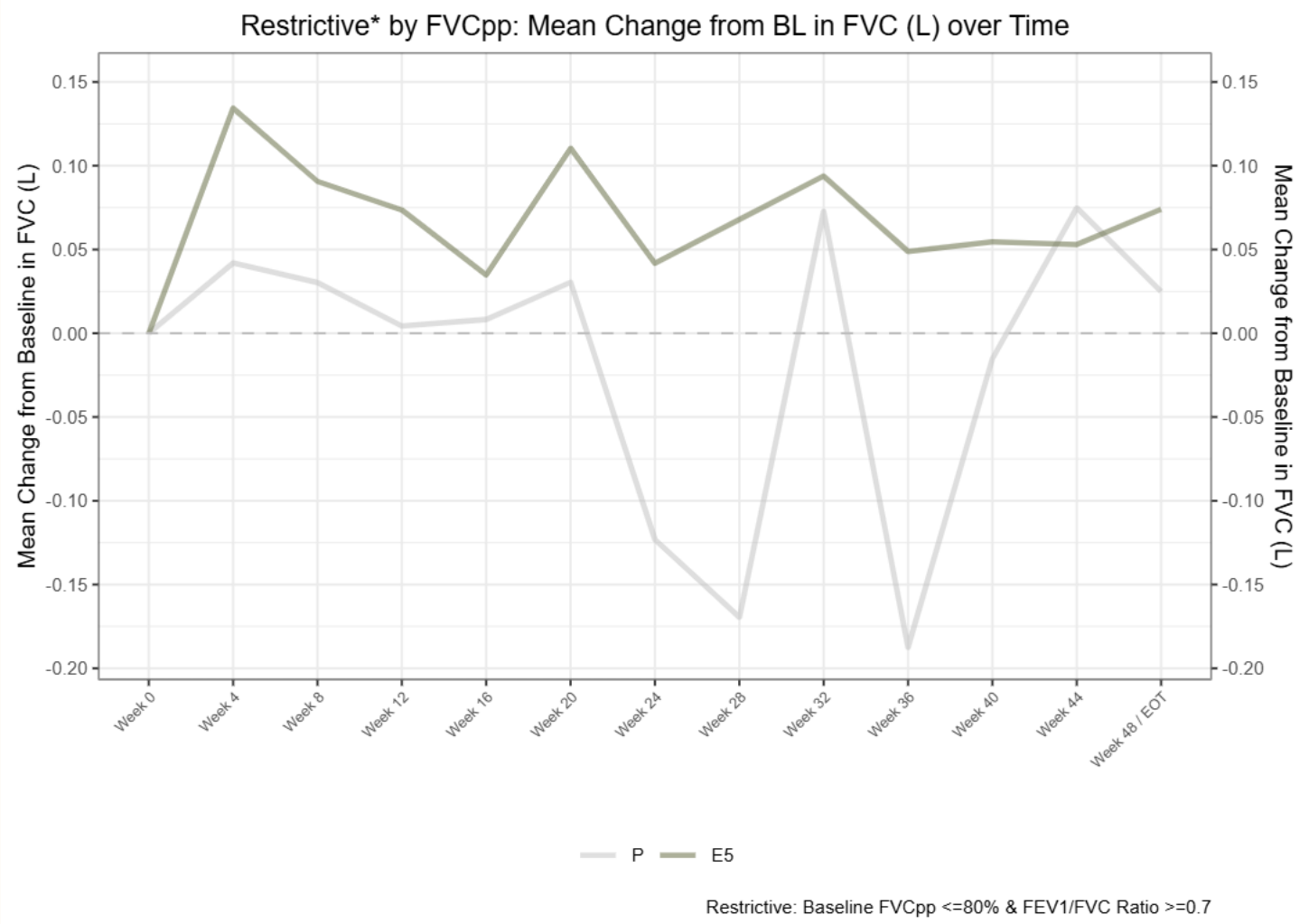


Patient-level Changes from BL over Time

MMRM: Within-Group LS Means over Time

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Restrictive Population: FVC Change From Baseline Over Time



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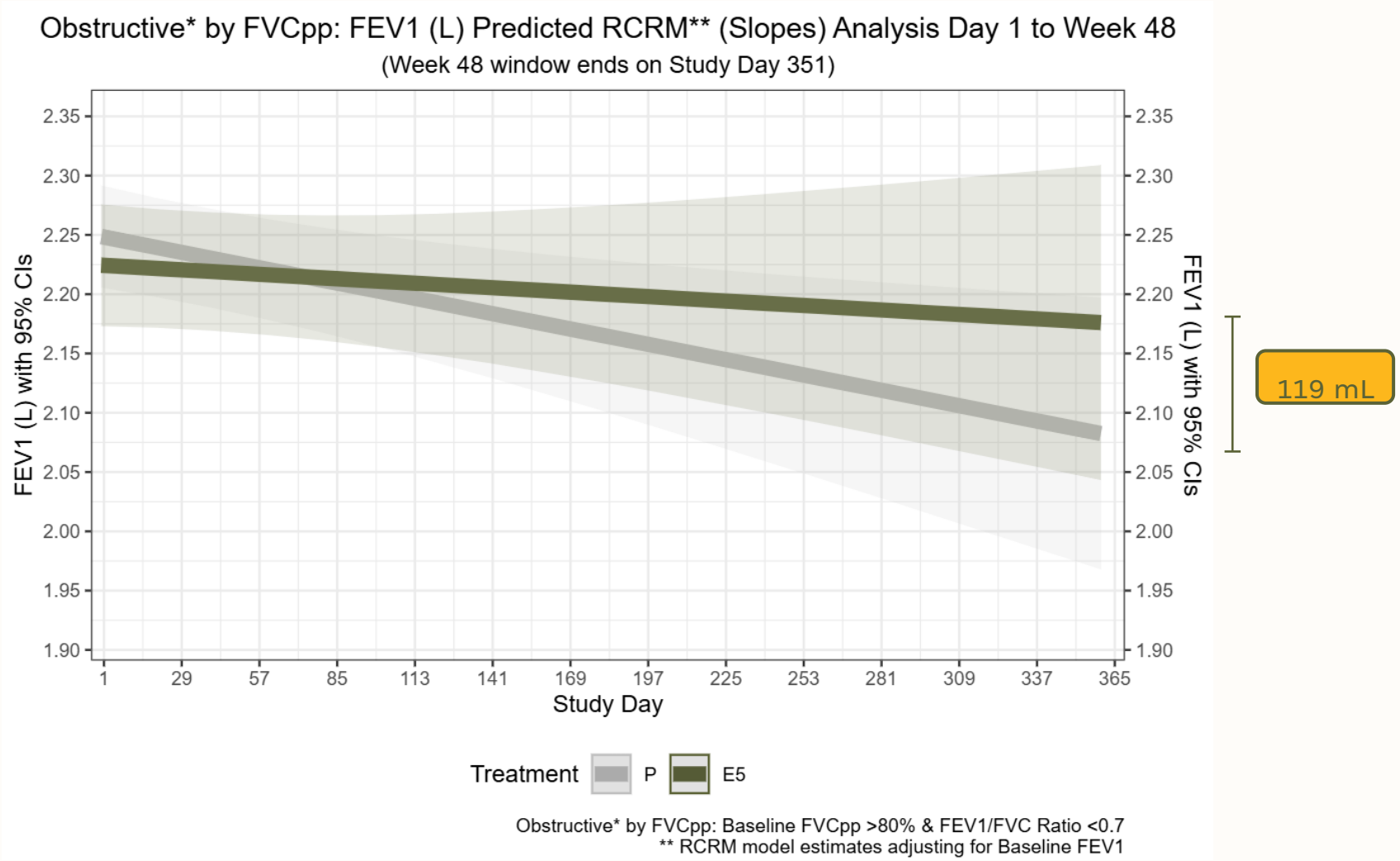
Spirometry: Summary

Subset	FVC W48 CFB Efzo vs pbo (ml)		FEV1 W48 CFB Efzo vs pbo (ml)	
	MMRM	RCRM	MMRM	RCRM
ITT	15.1*	34.2	27.4*	4.5
Restrictive	93.7	124	1.7	-4.3
Obstructive	95.4	187.7	100.3	119.4

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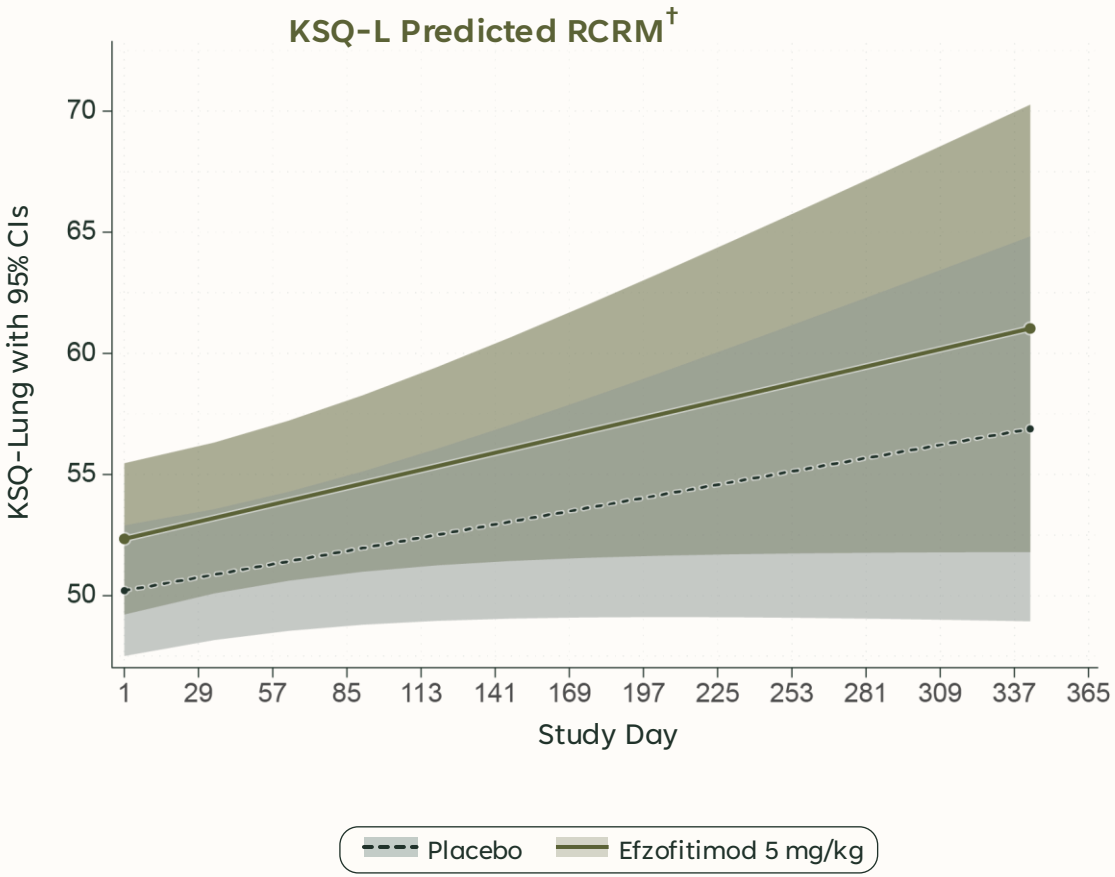
Obstructive Population: FEV1 RCRM

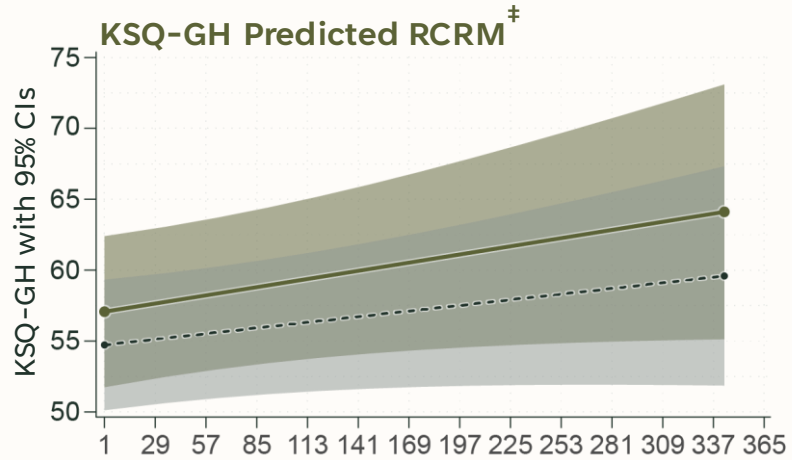
Trend toward benefit on FEV1 with Efzofitimod 5mg/kg

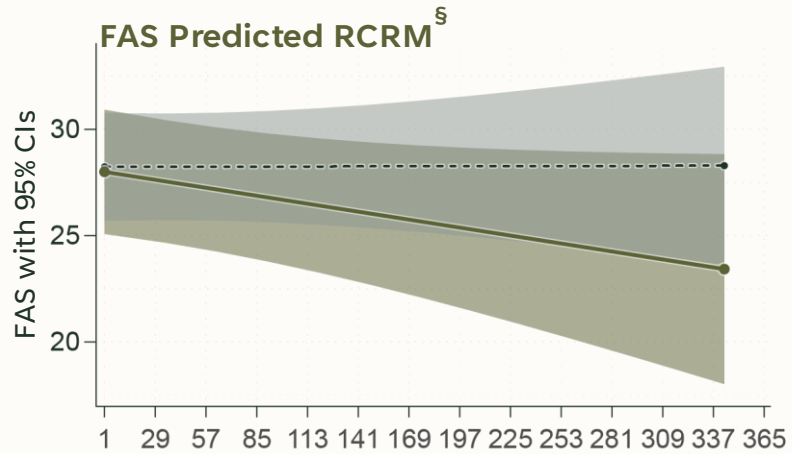


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Restrictive Population: Benefit on PROs Observed in EFZO-FIT in ITT Remains Consistent in Restrictive* Population





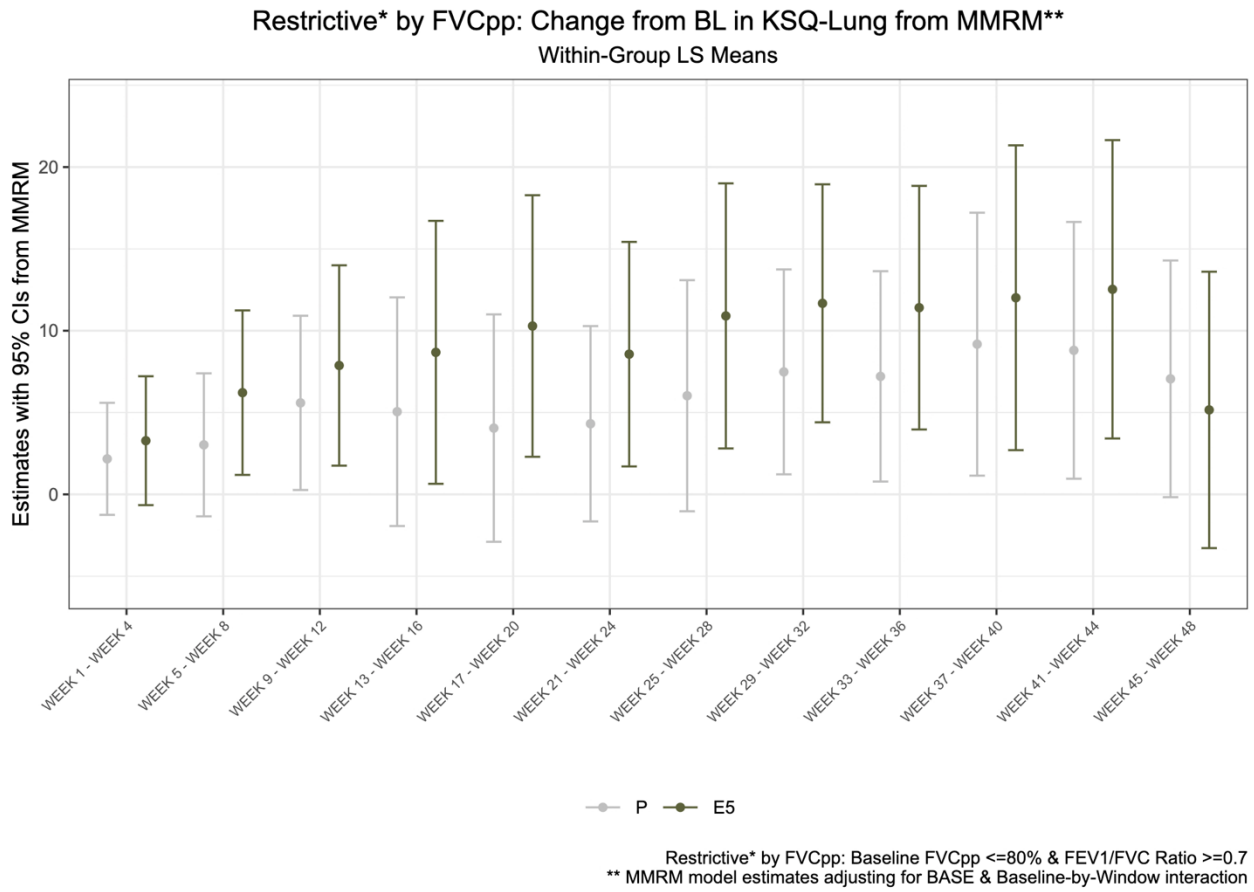


*Restrictive by FVCpp: Baseline FVCpp ≤80% & FEV1/FVC ration ≥0.7. †RCRM model est. adj. for Baseline MMLUNGSS. ‡RCRM model est. adj. for Baseline MMGENHSS. §RCRM model est. adj. for Baseline MMFASTOT. Week 48 window ends on Study Day 351. Abbreviations: CI, confidence interval; FAS, Fatigue Assessment Scale; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; FVCpp, forced vital capacity, percent predicted; ITT, intention-to-treat; KSQ-GH, King's Sarcoidosis Questionnaire-General Health; KSQ-L, King's Sarcoidosis Questionnaire-Lung; MMLUNGSS, baseline lung symptom score; MMFASTOT, baseline fatigue total score; MMGENHSS, baseline general health score; PRO, patient-reported outcome; RCRM, repeated continuous reassessment method.

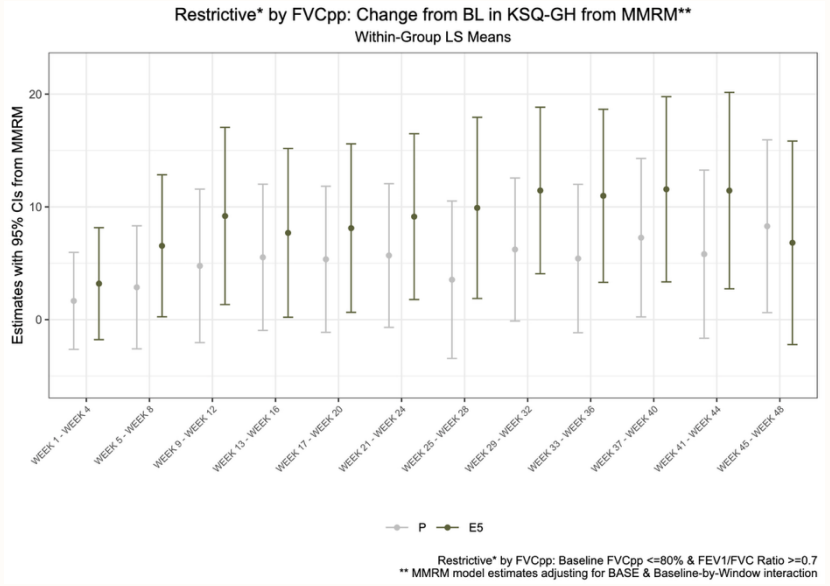
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Restrictive Population: Benefit on PROs Observed in EFZO-FIT in ITT Remains Consistent in Restrictive* Population

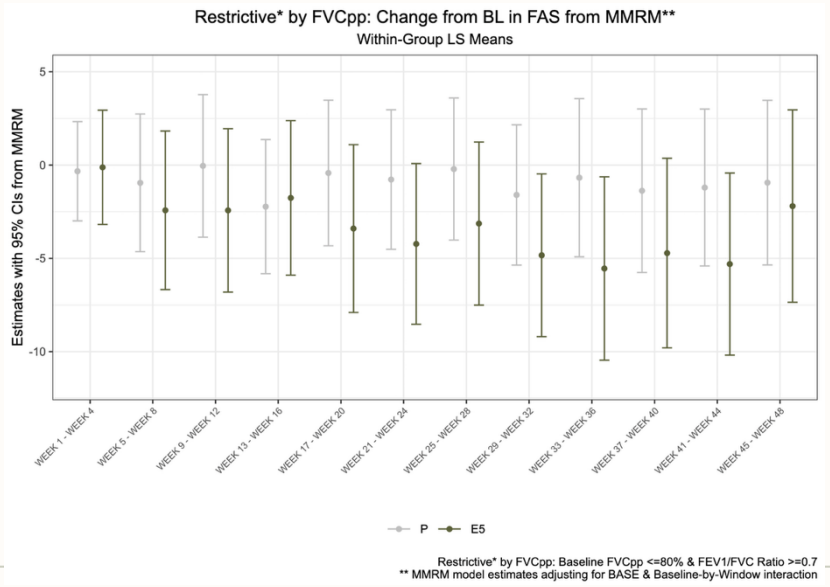
KSQ-L MMRM



KSQ-GH MMRM



FAS MMRM



*Restrictive by FVCpp: Baseline FVCpp ≤80% & FEV1/FVC ration ≥0.7

MMRM: Within-Group LS Means over Time

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Restrictive Population: Safety

No evidence for a dose dependent safety signal

	Placebo N = 16 n (%)	3 mg/kg N = 16 n (%)	5 mg/kg N = 12 n (%)
Any TEAEs	13 (81.3)	16 (100)	11 (91.7)
Any Serious TEAE (TESAEs)	2 (12.5)	4 (25)	2 (16.7)
TEAEs leading to study treatment discontinuation		1 (6.3)	3 (25)
Any SAEs leading to death		1 (6.3)	

There was no evidence for a dose dependent safety signal. The AE profile was generally similar to that seen for the ITT population with the exception that AEs such as wheezing (consistent with an obstructive phenotype) were not reported in any treatment arm in the restrictive subset.

A TEAE is defined as an adverse event that occurs on or after the first dose of study treatment.
A patient can be counted more than once across different categories.

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Restrictive Population: Prior Concomitant and New Concomitant Sarcoidosis - Immunosuppressants

Immunosuppressant use balanced between groups

Immunosuppressants	Placebo N = 16 n (%)	3 mg/kg N = 16 n (%)	5 mg/kg N = 12 n (%)
Immunosuppression by stratification	9 (56.3)	7 (43.8)	6 (50)
Prior Concomitant Sarcoidosis			
Methotrexate	8 (50)	3 (18.8)	5 (41.7)
Azathioprine	0	3 (18.8)	1 (8.3)
Mycophenolate mofetil	1 (6.3)	1 (6.3)	0
New Concomitant Sarcoidosis			
Methotrexate	2 (12.5)	1 (6.3)	1 (8.3)
Methotrexate sodium	0	1 (6.3)	0

Patients are counted only once within each Anatomical Therapeutic Chemical Level and Preferred Name.
Prior Concomitant - Medications if they were started before the first dose of study drug and were ongoing after the first dose of study drug.
New Concomitant – Medications if they were started after the first dose of study drug.

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Effect Estimate for FVC: Regulatory Precedence in ILD with Primary Measuring FVC

	Nintedanib (IPF)	Nintedanib (SSc-ILD)	Nerandomilast (IPF) 18 mg BD	Nerandomilast (IPF) 9 mg BD	Nerandomilast (PPF) 18 mg BD	Nerandomilast (PPF) 9 mg BD
Phase 3 trials	INPULSIS-1	SENSCIS	FIBRONEER™-IPF	FIBRONEER™-IPF	FIBRONEER™-ILD	FIBRONEER™-ILD
Baseline FVC Rx arm (SEM/SD) (ml)	2757± 735	2459 ± 736	2827±758	2837±781	2381±723	2326±768
Baseline FVC Pbo arm (SEM/SD) (ml)	2845 ± 820	2541 ± 816	2864±805	2864±805	2354±766	2354±766
CFB Rx (ml)	-94.5 //–114.7	–54.6//–52.4	–114.7	–138.6	–98.6	–84.6 ml
CFB Pbo (ml)	-205.0//–239.9	–101.0//–93.3	–183.5	–183.5	–165.8	–165.8
Pbo adjusted diff, 95% CI (ml)	110.6 (83.2,137.9)	46.4 (8.1 to 84.7)	68.8 (30.3 to 107.4)	44.9 (6.4 to 83.3)	67.2 (31.9 to 102.5)	81.1 (46.0 to 116.3)

EFZO-FIT restrictive phenotype effect sizes: RCRM 124 mL, MMRM 93 mL; sample size estimate 80 mL for the next Ph3

Richeldi L et al, NEJM 2014; Distler O et al, NEJM 2019; Richeldi L et al, NEJM 2025; Maher TM et al, NEJM 2025

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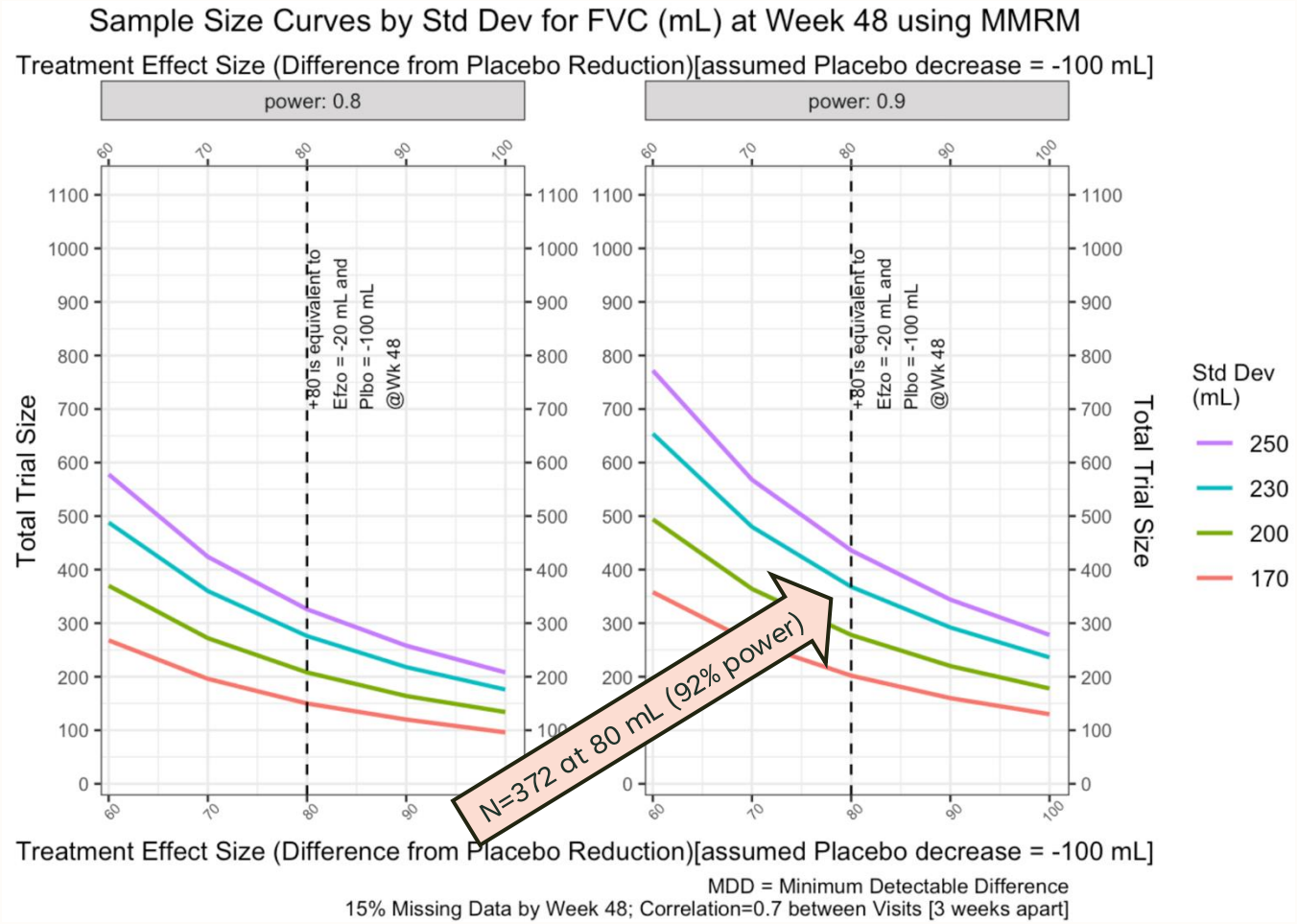
Sample Size Justification for C-006: FVC (mL)

“Variable” assumptions:

- Placebo-adjusted treatment effect:
  - Target = 80 mL “What we expect to achieve” (p-value will be ≤0.05)
  - Std Dev = 230

NOTE:

- MDD = 48 mL (Minimal Detectable Difference), i.e. a treatment effect that has p=0.05 (exactly). Corresponds to 50% power



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Thank You

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