ERS CONGRESS | 2025
27 September – 1 October | Amsterdam, Netherlands

# EFZO-FIT: The Largest Ever Interventional Trial in Pulmonary Sarcoidosis

Daniel Culver, DO
Cleveland Clinic
On behalf of the EFZO-FIT investigators

# Conflict of interest disclosure



❑ I have no real or perceived conflicts of interest that relate to this presentation.

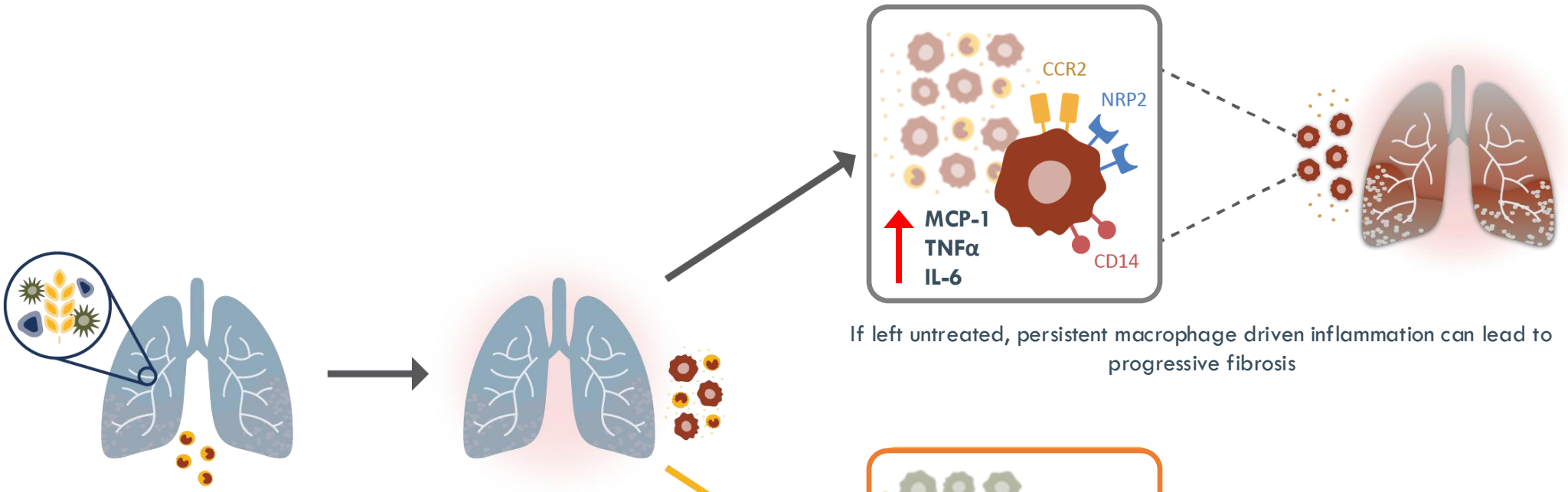
☒ I have the following real or perceived conflicts of interest that relate to this presentation:

| Affiliation / Financial interest | Commercial company |
|---|---|
| Grants/research support: | aTyr (institutional); Molecure (institutional); Boehringer-Ingelheim (institutional); Foundation for Sarcoidosis Research (institutional); NIH (institutional); |
| Honoraria or consultation fees: | Merck; Boehringer-Ingelheim; Foresee |
| Participation in a company sponsored bureau: | Pliant |
| Stock shareholder: | n/a |
| Spouse / partner: | n/a |
| Other support / potential conflict of interest: | n/a |

This event is accredited for CME credits by EBAP and speakers are required to disclose their potential conflict of interest. The intent of this disclosure is not to prevent a speaker with a conflict of interest (any significant financial relationship a speaker has with manufacturers or providers of any commercial products or services relevant to the talk) from making a presentation, but rather to provide listeners with information on which they can make their own judgments. It remains for audience members to determine whether the speaker's interests, or relationships may influence the presentation. The ERS does not view the existence of these interests or commitments as necessarily implying bias or decreasing the value of the speaker's presentation. Drug or device advertisement is forbidden.

# Efzofitimod Mechanism of Action

ERS CONGRESS | 2025
27 September – 1 October | Amsterdam, Netherlands




Immune triggers recruit monocytes, which differentiate to pro-inflammatory macrophages expressing NRP2

If left untreated, persistent macrophage driven inflammation can lead to progressive fibrosis

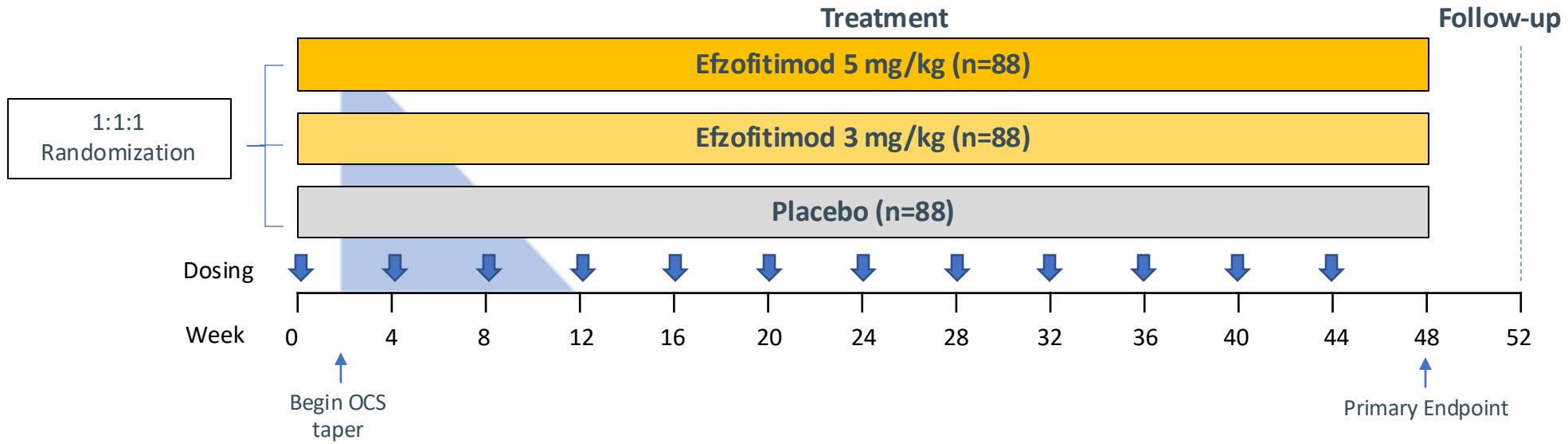
Efzofitimod acts as an NRP2 agonist

Efzofitimod promotes a less inflammatory macrophage population by downregulating key drivers of inflammation and fibrosis

Nangle et al. *Science Translational Medicine* 2025

# EFZO-FIT Study Design

ERS CONGRESS 2025
27 September – 1 October | Amsterdam, Netherlands




## Population

Diagnosis of pulmonary sarcoidosis for ≥6 months

Stable treatment with ≥ 7.5 and ≤ 25 mg/day OCS

1 immunosuppressant allowed

## Endpoints

Primary:

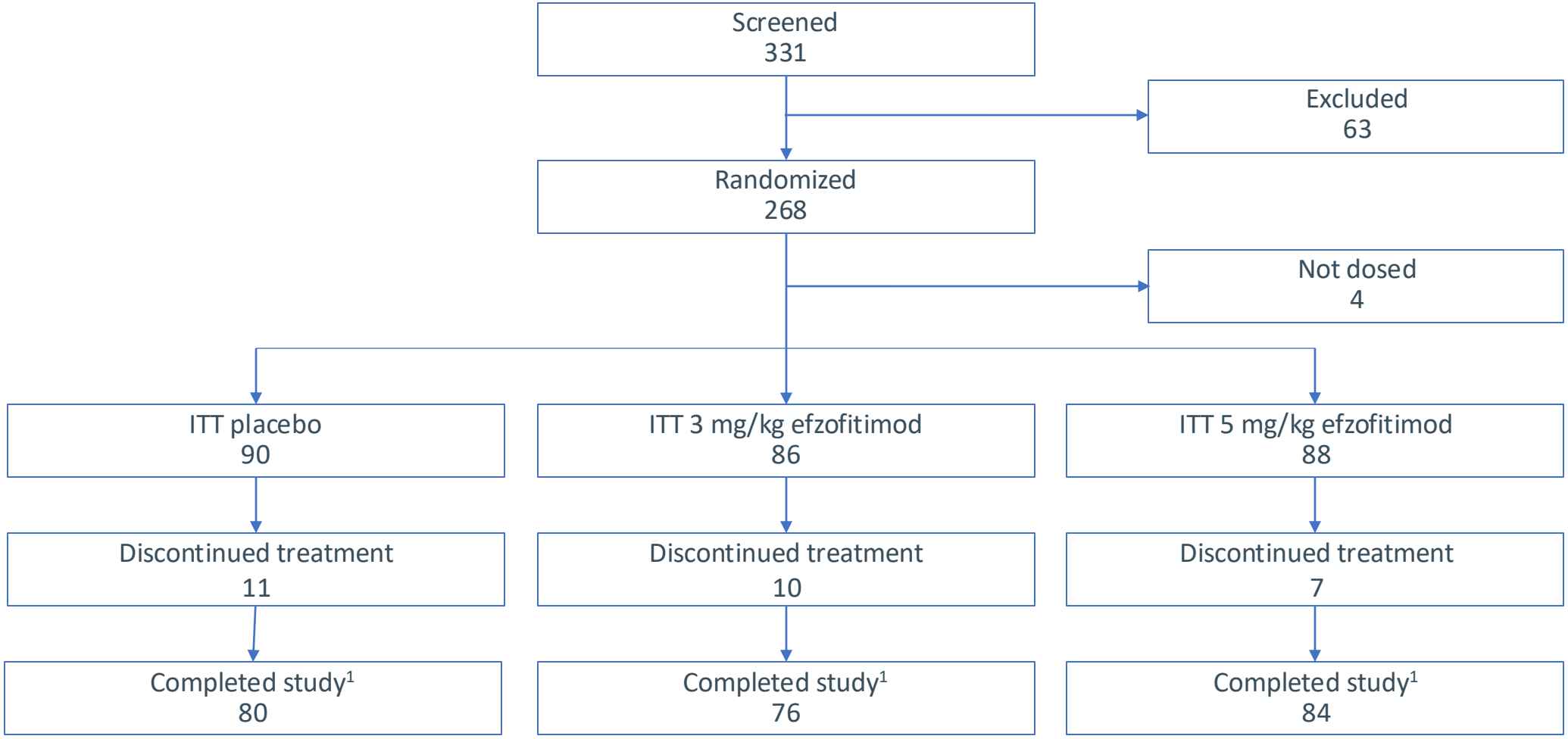
Change from baseline in mean daily OCS dose at Week 48

Secondary:

Steroid withdrawal; KSQ-Lung; FVC

# Study Disposition

ERS CONGRESS 2025
27 September – 1 October | Amsterdam, Netherlands




[1]Completed at least 10 doses and completed follow Up

# Baseline Characteristics

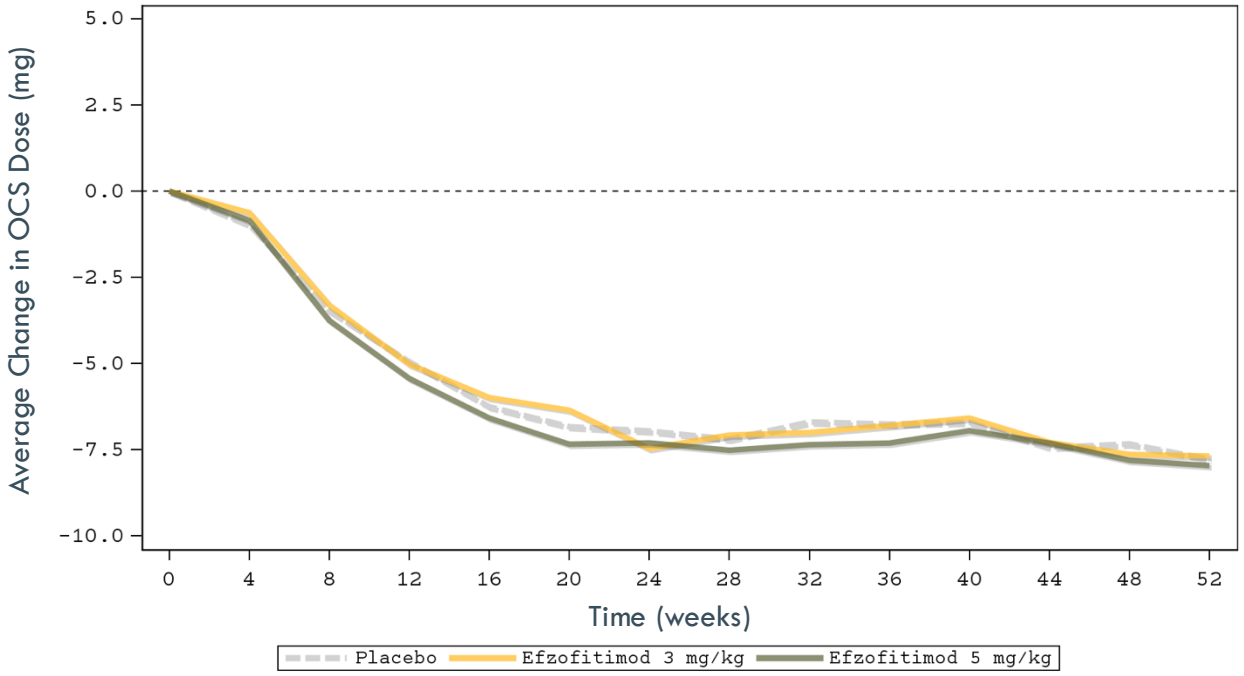


| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| Age (Years); mean (SD) | 54.1 (10.5) | 54.5 (11.9) | 52.7 (9.2) |
| Sex (Male); n (%) | 56 (62.2) | 47 (54.7) | 47 (53.4) |
| Race | | | |
| Black / African American; n (%) | 15 (16.7) | 12 (14.0) | 16 (18.2) |
| Asian; n (%) | 15 (16.7) | 11 (12.8) | 10 (11.4) |
| Duration of disease (Years); mean (SD) | 8.7 (9.1) | 8.7 (8.2) | 7.0 (6.3) |
| Extrapulmonary sarcoidosis; n (%) | 29 (32.2) | 28 (32.6) | 28 (31.8) |
| KSQ-Lung score; mean (SD) | 49.4 (9.1) | 53.5 (11.5) | 51.6 (10.7) |
| FVC % predicted; mean (SD) | 89.2 (17.4) | 86.5 (15.4) | 90.7 (17.5) |
| Pulmonary phenotype; n (%) | | | |
| Obstructive / Mixed | 38 (42.2) | 32 (37.2) | 30 (34.1) |
| Steroid dose (mg/day); mean (SD) | 10.7 (4.7) | 10.5 (4.0) | 10.7 (4.6) |
| Duration of OCS; mean (SD) | 4.6 (5.6) | 4.5 (5.6) | 4.6 (5.0) |
| Immunosuppressant; n (%) | 34 (37.8) | 33 (38.4) | 32 (36.4) |

# Change from Baseline in OCS



## Average Change from Baseline in OCS Dose Over Time




## OCS Dose at Week 48

| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| LS mean dose at week 48 (mg) | 3.5 | 3.5 | 2.8 |
| LS mean change from baseline (mg) | -7.1 | -7.1 | -7.9 |
| Difference in LS mean (95% CI) | - | 0.0 (-1.5, 1.5) | -0.7 (-2.2, 0.8) |
| *p-value* | - | *0.9804* | *0.3313* |

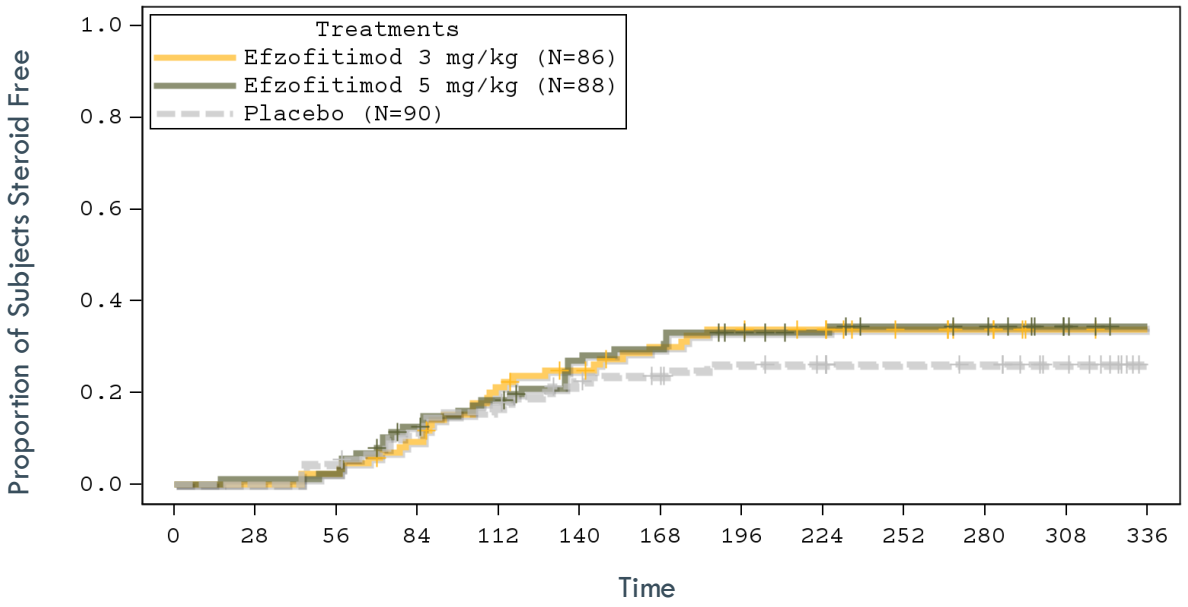
# Steroid Withdrawal



## Steroid Free at Week 48

| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| Steroid free[1]; 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) |
| *Nominal p-value* | - | *0.1172* | *0.0919* |

## Kaplan Meier Curve of Time to Steroid Free Sustained for 180 Days




[1]Missing patients considered non-responders

# King's Sarcoidosis Questionnaire-Lung

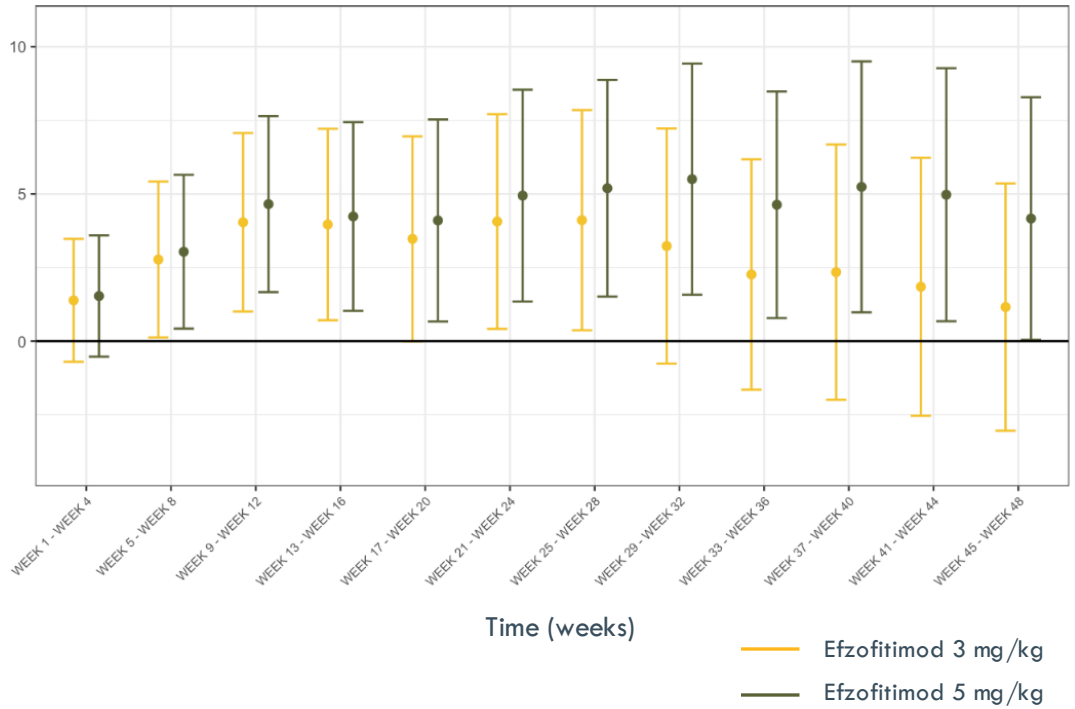


## Change from Baseline in KSQ-L at Week 48

| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| LS mean change from baseline | 6.2 | 7.3 | 10.4 |
| Difference; LS mean (95% CI) | - | 1.1 (-3.1, 5.4) | 4.2 (0.0, 8.3) |
| *Nominal p-value* | - | *0.5932* | ***0.0479*** |

Ongoing KSQ-L validation work conducted by aTyr supports a MCID for improvement between groups of 2.1 points

## Differences in KSQ-L Change from Baseline vs Placebo*

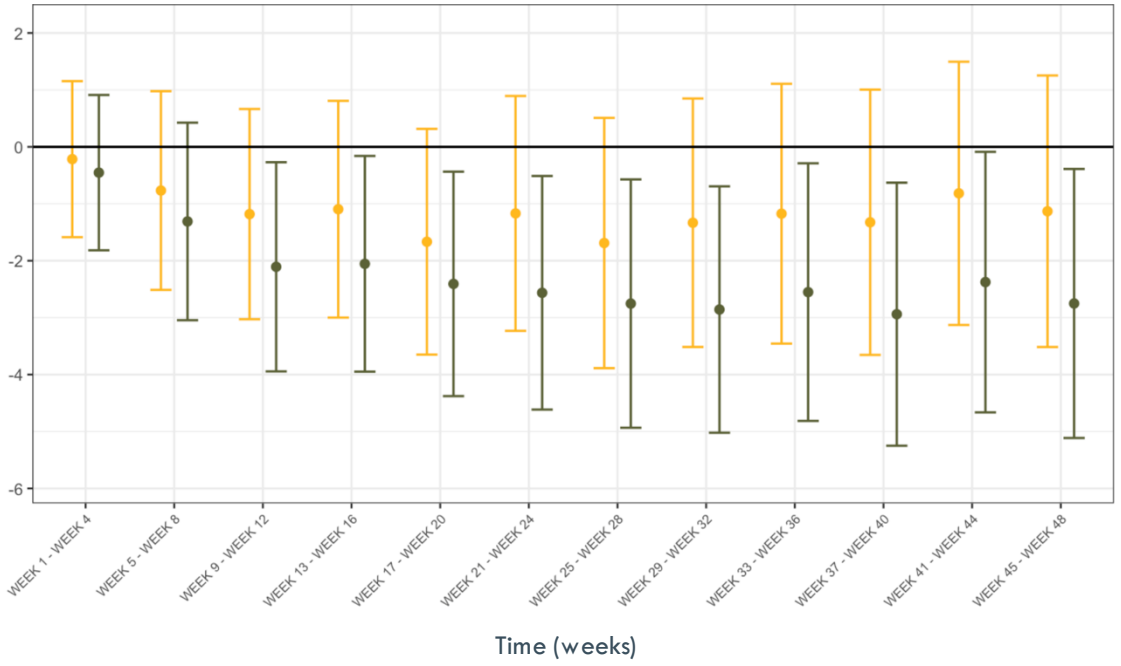



*LS Means

# Consistent Benefit Observed on QOL

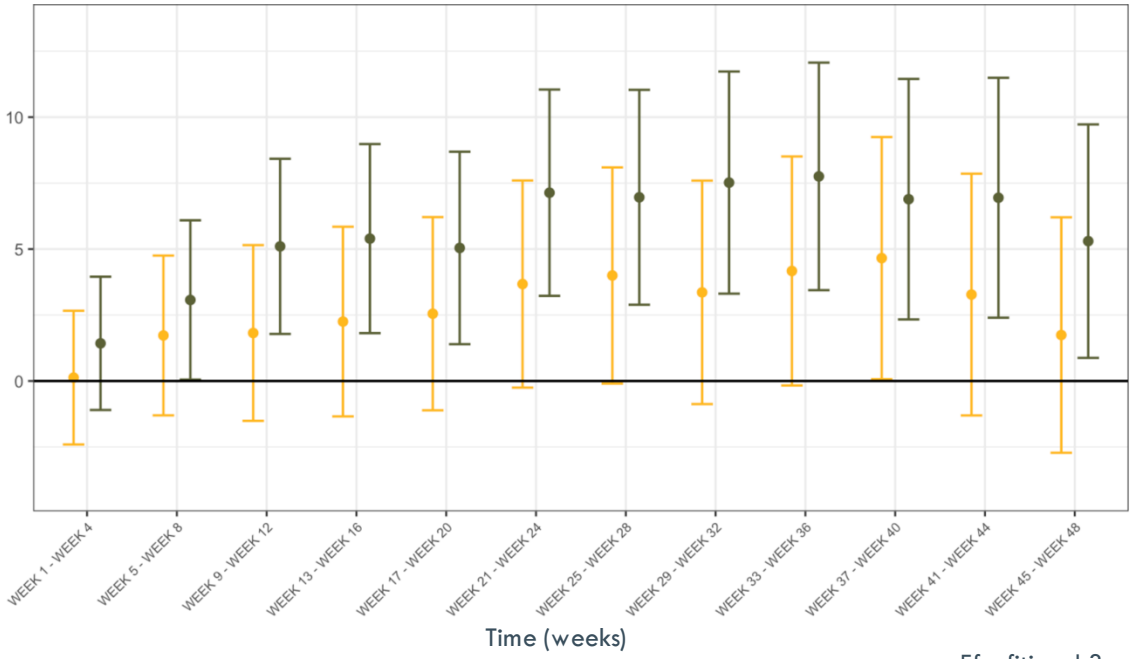
ERS CONGRESS 2025
27 September – 1 October | Amsterdam, Netherlands

## Differences in FAS Total Score Change from Baseline vs Placebo*




*Week 48 difference in LS mean change from baseline nominal p-value = **0.0226***

## Differences in KSQ-GH Change from Baseline vs Placebo*




*Week 48 difference in LS mean change from baseline nominal p-value = **0.0197***

*LS Means; FAS = Fatigue Assessment Scale; KSQ-GH = King's Sarcoidosis Questionnaire – General Health

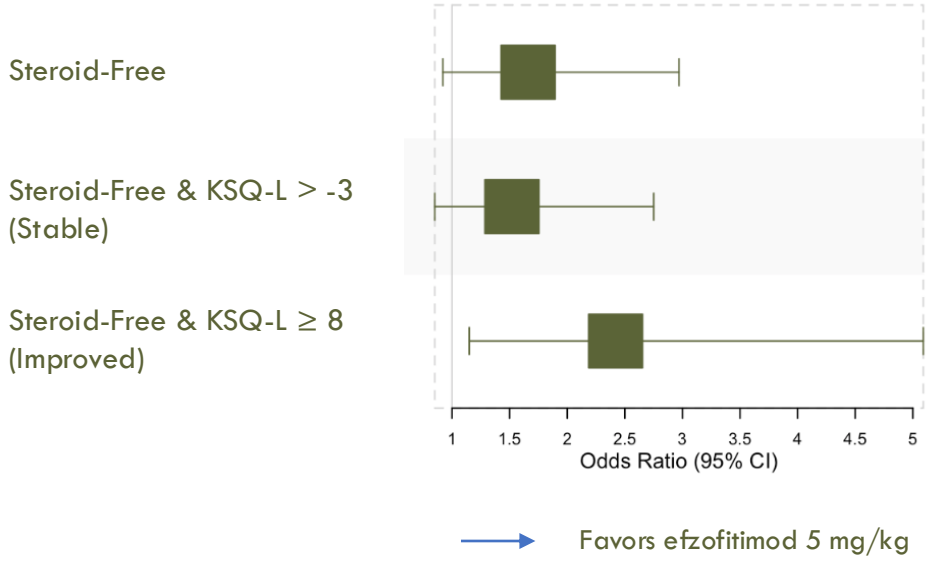
# King's Sarcoidosis Questionnaire-Lung / Steroid Free Composites

ERS CONGRESS | 2025
27 September – 1 October | Amsterdam, Netherlands

## Steroid Free and KSQ-L Composite Endpoints

| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| Steroid free and stable KSQ-L; n (%) [1] | 33 (36.7) | 41 (47.7) | 41 (46.6) |
| Odds ratio (95% CI) | - | 1.6 (0.8, 2.9) | 1.6 (0.8, 2.9) |
| *Nominal p-value* | - | *0.1592* | *0.1607* |
| Steroid free and improved KSQ-L; n (%) [1] | 13 (14.4) | 24 (27.9) | 26 (29.5) |
| Odds ratio (95% CI) | - | 2.2 (1.1, 4.8) | 2.4 (1.2, 5.2) |
| *Nominal p-value* | - | ***0.0381*** | ***0.0196*** |

## Efzofitimod 5 mg/kg vs Placebo from Logistic Regression




[1]Missing patients treated as non-responders

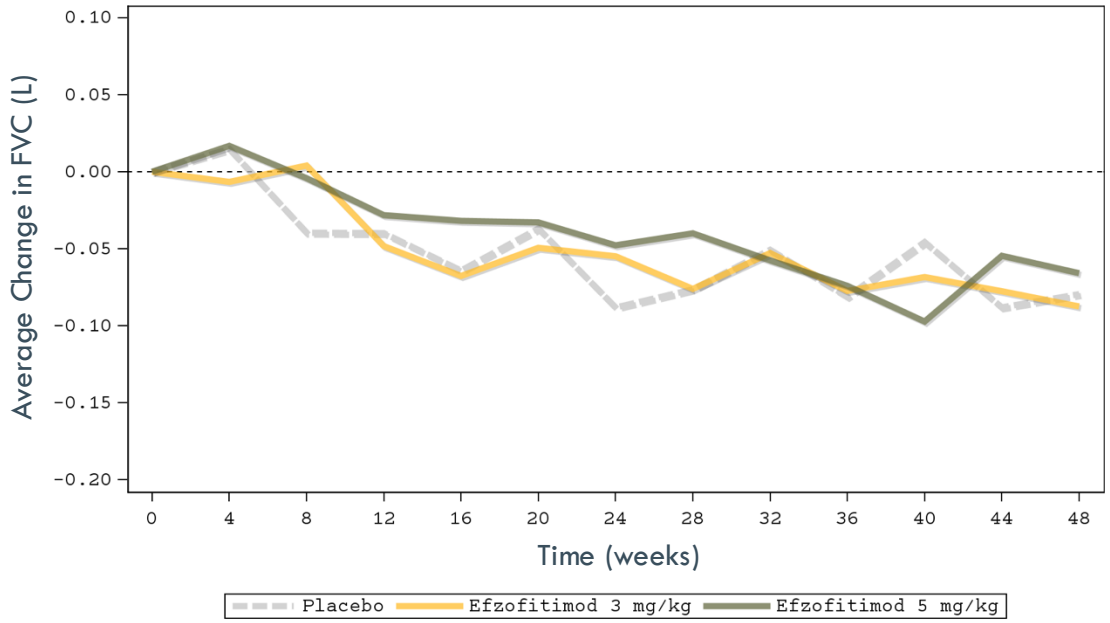
# Forced Vital Capacity (FVC)



## FVC at Week 48 (MMRM)

| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| FVC (mL), LS mean at week 48 | 3380.4 | 3369.7 | 3395.4 |
| LS mean change from baseline (mL) | -84.5 | -95.1 | -69.4 |
| Difference in LS means (mL) | - | -10.6 | 15.1 |
| 95% CI | - | -104.7, 83.5 | -77.4, 107.6 |
| *Nominal p-value* | - | *0.8244* | *0.7485* |

## Change from Baseline in FVC (L) over Time



# Summary of SAE, AE Discontinuations and ADA



| | Placebo N=90 | Efzofitimod 3 mg/kg N=86 | Efzofitimod 5 mg/kg N=88 |
|---|---|---|---|
| SAE | 10 | 12 | 7 |
| Treatment related (per PI) | 2 (pneumonia, scrotal abscess) | 2 (PPF, RSV infection) | 1 (pneumonia) |
| Discontinuations due to AE | 4 | 3 | 4 |
| Treatment related (per PI) | 2 (hypersensitivity, hypotension) | 1 (PPF) | 1 (CIDP) |
| Anti-drug antibody | | | |
| Treatment induced | 1 | 1 | 3 |
| Treatment boosted | 1 | 0 | 0 |

# Conclusions



- EFZO-FIT is the largest-ever RCT in sarcoidosis
- Pulmonary sarcoidosis patients can be managed for prolonged periods with lower steroid doses than we are currently using
- Efzofitimod is safe and well-tolerated
- The trial did not meet its primary endpoint (change from baseline in mean daily steroid dose at week 48)
- Positive signals were observed for several PROs, as well as freedom from steroids
  - Pre-specified PROs (KSQ-L, KSQ-GH, FAS) had nominal p value $< 0.05$
- Additional analyses are underway

# ERS CONGRESS | 2025

27 September – 1 October | Amsterdam, Netherlands