



A New Path to Medicine

H.C. Wainwright 24th Annual Global Investment Conference

Sanjay S. Shukla, M.D., M.S.

President and CEO

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Forward Looking Statements

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aTyr: A New Path to Medicine

Mission: Translate discoveries from our tRNA synthetase platform into new therapeutics for fibrosis, inflammation and cancer

Efzofitimod (ATYR1923)

- Immunomodulator with novel MOA for fibrotic lung disease
- Favorable safety profile to date
- Clinical POC in pulmonary sarcoidosis supports program advancement and expansion to other ILD

Lead Indication: Pulmonary Sarcoidosis

- Major form of ILD with limited treatment options and poor outcomes for many patients
- Orphan drug and Fast Track designations granted
- Positive Phase 1b/2a data for efzofitimod reported Sept. 2021
- Global pivotal Phase 3 EFZO-FIT™ study recently initiated

Platform and Target Validation

- Efzofitimod clinical POC validates tRNA synthetase platform and NRP2 as a therapeutic target
- NRP2 antibody ATYR2810 in pre-clinical development for cancer
- Discovery of FGFR4 as target receptor for AARS fragment
- Future tRNA synthetase discovery work progressing

Financials: Cash, cash equivalents and investments at \$89.3m as of June 30, 2022

aTyr Development Pipeline

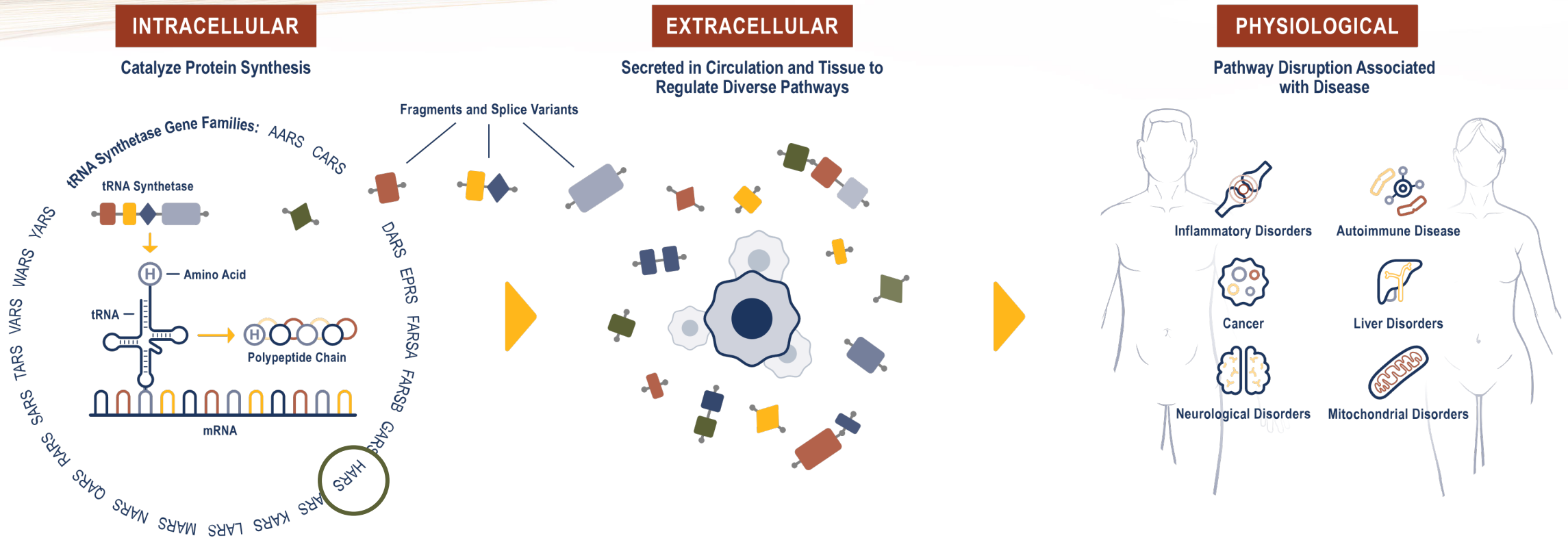
PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
	Pulmonary Sarcoidosis					
Efzofitimod (ATYR1923)	Other ILDs (CTD-ILD; CHP) ⁽¹⁾					
	Healthy Japanese Volunteers ⁽²⁾					
ATYR2810	Solid Tumors					
NRP2 mAbs	Cancer; Inflammation					
AARS-1; DARS-1⁽³⁾	Cancer; Fibrosis; Inflammation					

(1) CTD-ILD: connective tissue disease-related ILD (e.g. Scleroderma-related ILD); CHP: chronic hypersensitivity pneumonitis

(2) In partnership with Kyorin Pharmaceutical Co., Ltd. Kyorin's Phase 1 study in healthy Japanese volunteers has been completed. Kyorin is eligible to participate in future efzofitimod trials sponsored by aTyr.

(3) The next two candidates from our tRNA synthetase platform; initial focus on NK cell biology

Foundational Science: Novel Functions of Extracellular tRNA Synthetases



tRNA synthetases are secreted extracellularly and occur in novel forms which lose their canonical function

Extracellular tRNA synthetase disruption (genetic/autoimmune) is associated with disease in humans

Validated synthetase platform is an engine for new protein therapeutics (e.g. efzofitmod) and new target identification (e.g. NRP2)

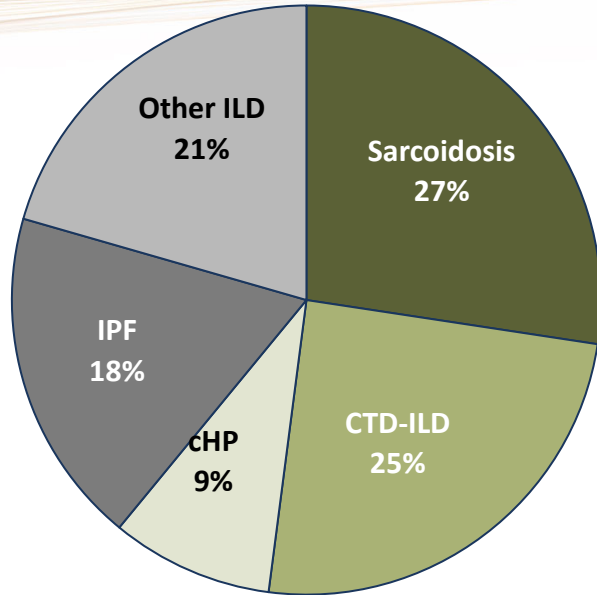


Efzofitimod (ATYR1923)

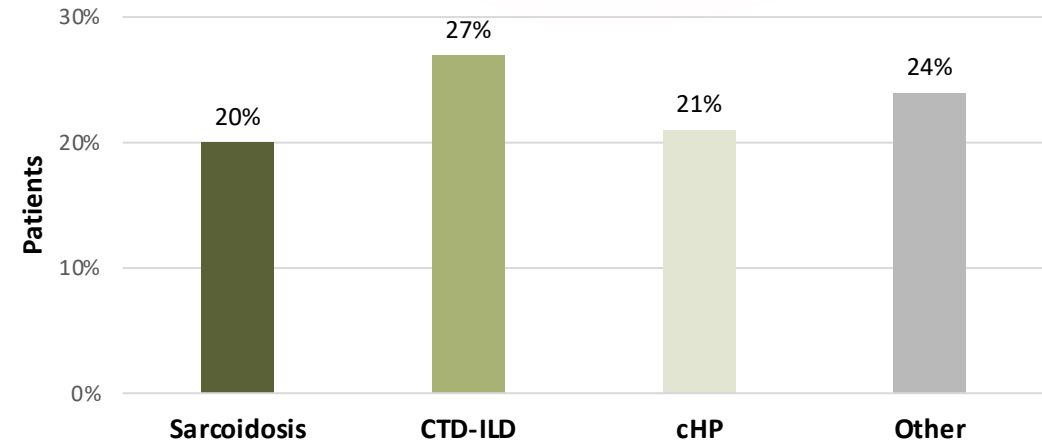
A Novel Immunomodulator for Fibrotic Lung Disease

ILD: Immune-mediated Fibrotic Lung Diseases with Poor Outcomes

ILD Types



Patients with Fibrosis (non-IPF)¹



- >200 types: 4 main ILDs comprise ~80% of patients
- Immune pathology common to non-IPF ILD – fibrosis occurs in >20%
- Limited treatment options
- **\$2-3B global peak sales** opportunity in non-IPF ILD

Pulmonary Sarcoidosis: The Most Prevalent ILD

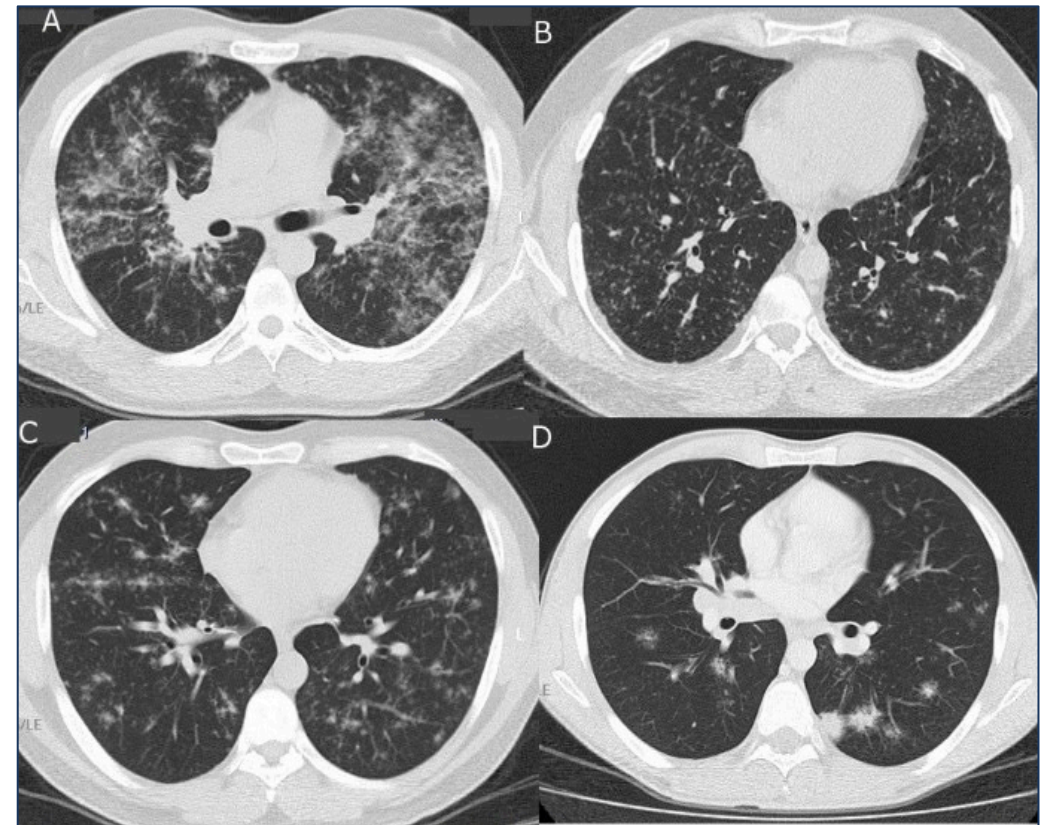
- Inflammatory disease of unknown etiology, characterized by presence of granulomas in one or more organs
- Lung affected in >90% of patients
- 1 in 5 patients develop lung fibrosis, significantly worsening prognosis
- Standard of care based on limited clinical evidence and associated with significant toxicity

Reasons to treat sarcoidosis

- 1) Avoid danger to organ(s)
- 2) Improve quality of life

U.S. FDA orphan drug designation for sarcoidosis and Fast Track designation for pulmonary sarcoidosis granted

Lung HRCT Showing Nodules and Ground Glass Opacity¹



Current SOC Has Limited Evidence of Efficacy and Poor Safety

Corticosteroids



Anti-metabolites immunosuppressants



Biologic immunomodulators



FDA approval

1950s

1980s*

2000s*



Severe weight gain
Mood disorders
Loss of bone density
Exacerbation of diabetes
Glaucoma
Hypertension

Infections
Liver toxicity
Bone marrow suppression

Tuberculosis
Malignancies

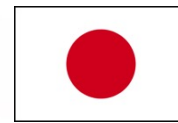
Significant Market Opportunity in Sarcoidosis Alone



200,000 patients

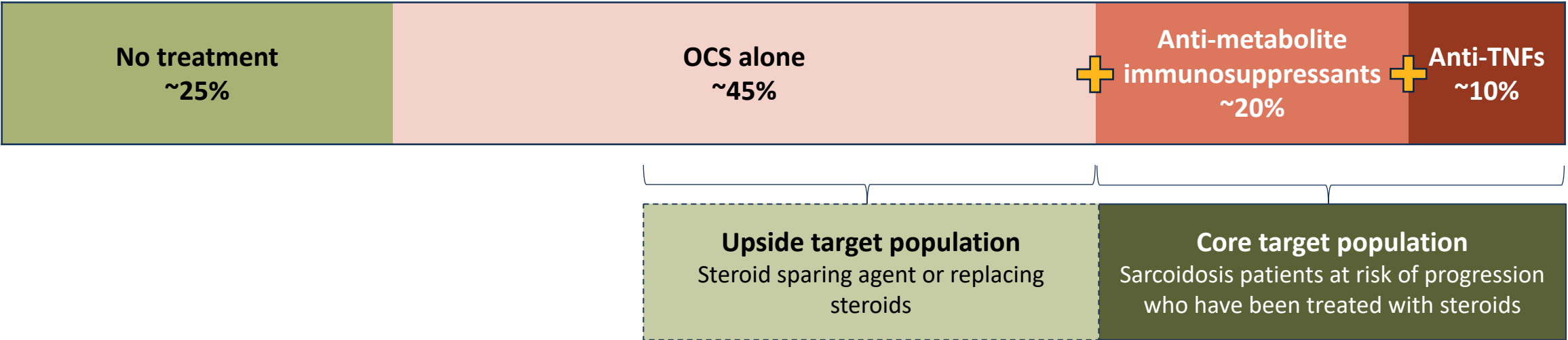


150,000 patients



20,000 patients

Patient Treatment Segmentation⁽¹⁾



Target efzofitimod population in major markets represents **150,000 – 200,000 patients**

Multiple Benchmarks Support Premium Price for Efzofitimod⁽¹⁾

~\$180K



HUMIRA
adalimumab

TAVNEOS
(avacopan)

Lupkynis
(voclosporin) capsules 7.9 mg

OFEV
nintedanib

Esbriet
(pirfenidone) tablets 267 mg 801 mg

ACTEMRA
tocilizumab

Remicade
INFLIXIMAB

ILD treatments that slow lung
function decline
(Ofev, Esbriet, Actemra)

Steroid sparing agents for rare
inflammatory disorders
(Tavneos, Lupkynis)

Biologic immunomodulators for
chronic inflammatory autoimmune
diseases used off-label in sarcoidosis
(Humira, Remicade)

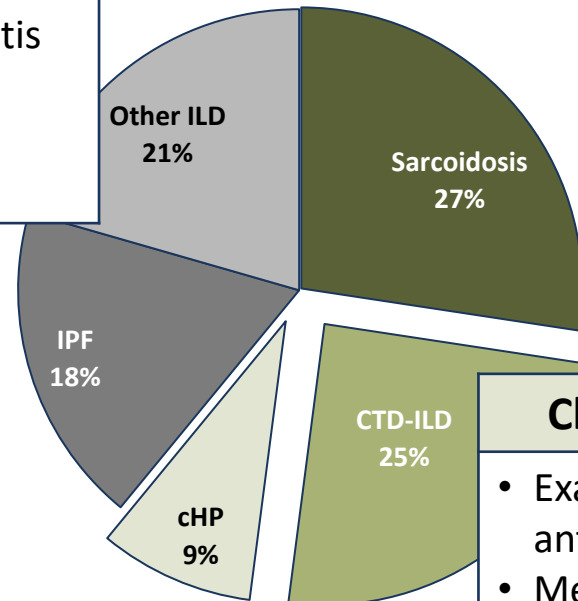
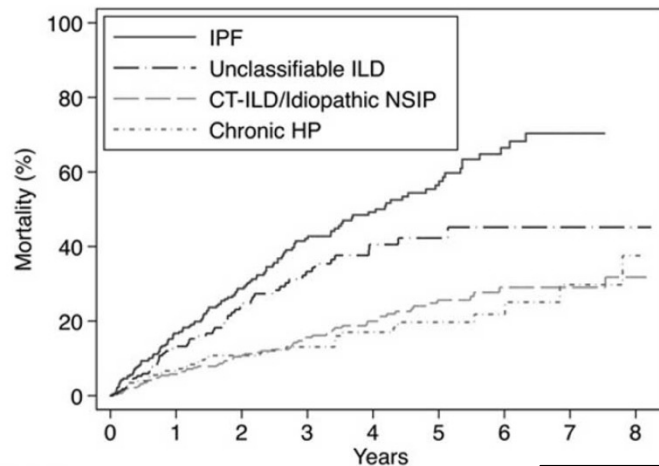
**Efzofitimod could be the first
approved product for a major ILD,
sarcoidosis, based on steroid
sparing, preserving lung function
and improving patient QoL**

Efzofitimod Data Supports Expansion to Other High Unmet Need ILDs

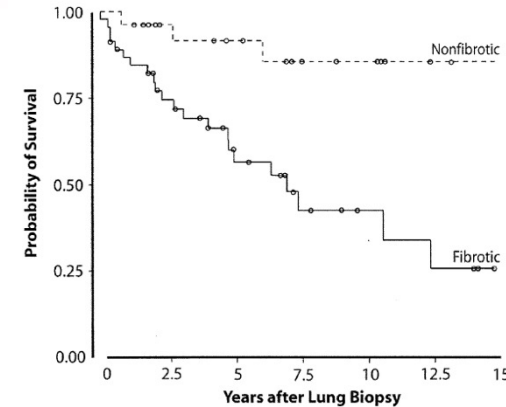
Connective Tissue Disease Related ILD (CTD-ILD)

- ILD secondary to autoimmune diseases, such as systemic sclerosis (SSc-ILD) or rheumatoid arthritis (RA-ILD)
- ILD is the leading cause of mortality
- Similar standard of care to sarcoidosis

High Mortality Burden in CTD-ILD and cHP¹



Fibrosis Drives Mortality²



Chronic Hypersensitivity Pneumonitis (cHP)

- Exaggerated chronic immune response to inhaled antigens
- Median survival of only ~7 years with no approved therapies
- Similar standard of care sarcoidosis

Efzofitimod: Potential First-in-Class Therapy for Immune-Mediated Lung Disease

MOA

- Targets innate and adaptive immune cells during active inflammation to restore immune balance via selective modulation of NRP2
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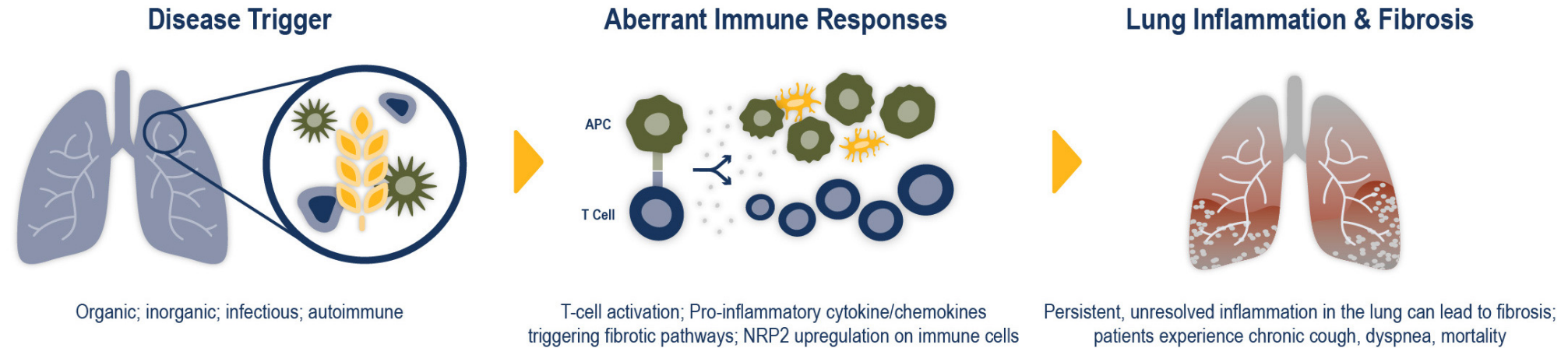
Pre-Clinical Evidence

- Anti-inflammatory and anti-fibrotic effects demonstrated in translational models of multiple ILDs
 - Reduces inflammatory cytokines and pro-fibrotic chemokines *in vitro* and *in vivo*
 - No toxicity observed in GLP toxicology rodents and non-human primates out to 6 months
-

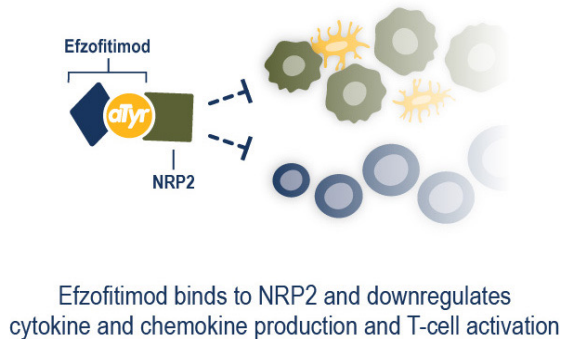
Clinical Experience

- Safe and well-tolerated in clinical trials to date with exposure to 24 weeks
- No immunogenicity observed
- Controls inflammation by downregulating cytokines implicated in sarcoidosis and other ILD
- Dose-dependent disease control demonstrated in pulmonary sarcoidosis patients

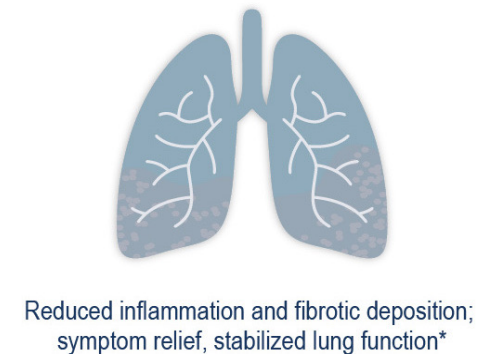
Efzofitimod Therapeutic Goal: Restore Immune Balance and Prevent Fibrosis



Efzofitimod Dampens Immune Responses



Stabilized Lung



*aTyr hypothesis

Phase 1b/2a Data Supports Proof-of-Concept and Clinical Advancement

- Efzofitimod was safe and well-tolerated
- Strong suggestion of efficacy: Dose-response and consistent positive trends across key efficacy endpoints and multiple analysis populations
- Clinically meaningful symptom improvements in dyspnea, cough, fatigue and King's Sarcoidosis scores
- Dose dependent control of inflammatory biomarkers confirms anti-inflammatory effect

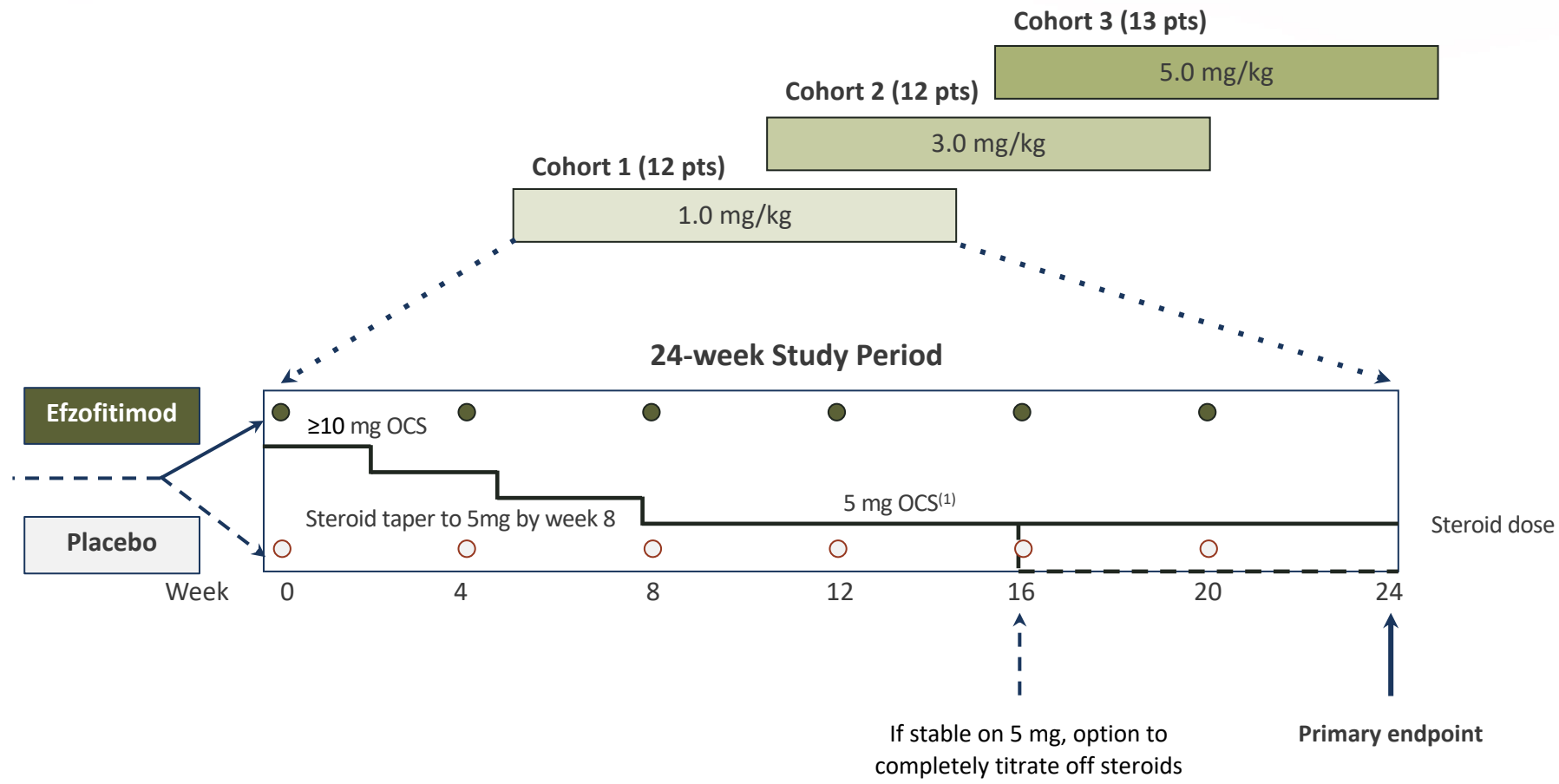
Platform and target validation

First tRNA synthetase derived and NRP2 targeting compound to demonstrate clinical POC

Trial Design

Design	• Randomized (2:1), double-blind, placebo-controlled, multiple ascending dose • 24 week study: 6 monthly IV doses of efzofitimod tested at 1.0, 3.0, and 5.0 mg/kg • Forced steroid taper to 5.0 mg by week 8; amendment to allow taper to 0 mg at week 16 in responders
Population	• 37 histologically confirmed pulmonary sarcoidosis patients • ≥ 10 mg stable oral corticosteroid treatment • Symptomatic/active disease at baseline
Primary Endpoint	• Safety and tolerability of multiple ascending IV efzofitimod doses
Secondary Endpoints	• Steroid-sparing effect • Immunogenicity • Pharmacokinetics (PK) • Exploratory: Lung function (FVC and other PFTs); sarcoidosis symptom scores and quality of life scales; inflammatory and sarcoidosis biomarkers; FDG-PET/CT imaging

Study Schema



Baseline Demographics and Disease Characteristics Generally Balanced

Demographics	Placebo N=12	Efzofitimid 1 mg/kg N=8	Efzofitimid 3 mg/kg N=8	Efzofitimid 5 mg/kg N=9
Age (Years); mean (SD), >=65	52.5 (10.2), 0	54.5 (11.3), 1	51.8 (11.4), 2	50.8 (9.2), 0
Sex (Male); n (%)	5 (42)	4 (50)	4 (50)	4 (44)
Race; White / African American	9 / 3	5 / 3	6 / 2	3 / 6
Disease characteristics Mean (SD)				
FVC (% predicted)	77.3 (11.5)	68.3 (9.7)	83.8 (7.3)	83.8 (16.6)
Duration of disease (Years)	4.2 (3.3)	7.4 (6.1)	5.9 (5.1)	7.7 (9.9)
Baseline Dyspnea Index Score	4.8 (2.0)	4.3 (1.8)	7.6 (3.0)	6.3 (2.5)
Background Therapy				
Steroid dose (mg/day), mean	13.3	11.3	14.4	13.9
Immunomodulator; n (%)	6 (50)	3 (38)	1 (13)	4 (44)

Monthly Dosing of Efzofitimod was Safe and Well-Tolerated

n (%)	Placebo N=12	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 5 mg/kg N=9
AEs	10 (83)	8 (100)	7 (88)	8 (89)
Drug-related AEs	4 (33)	3 (38)	1 (13)	3 (33)
Severe AEs (Grade 3 or 4)	4 (33)	2 (25)	0	2 (22)
SAEs	1 (8)	1 (13)	0	0

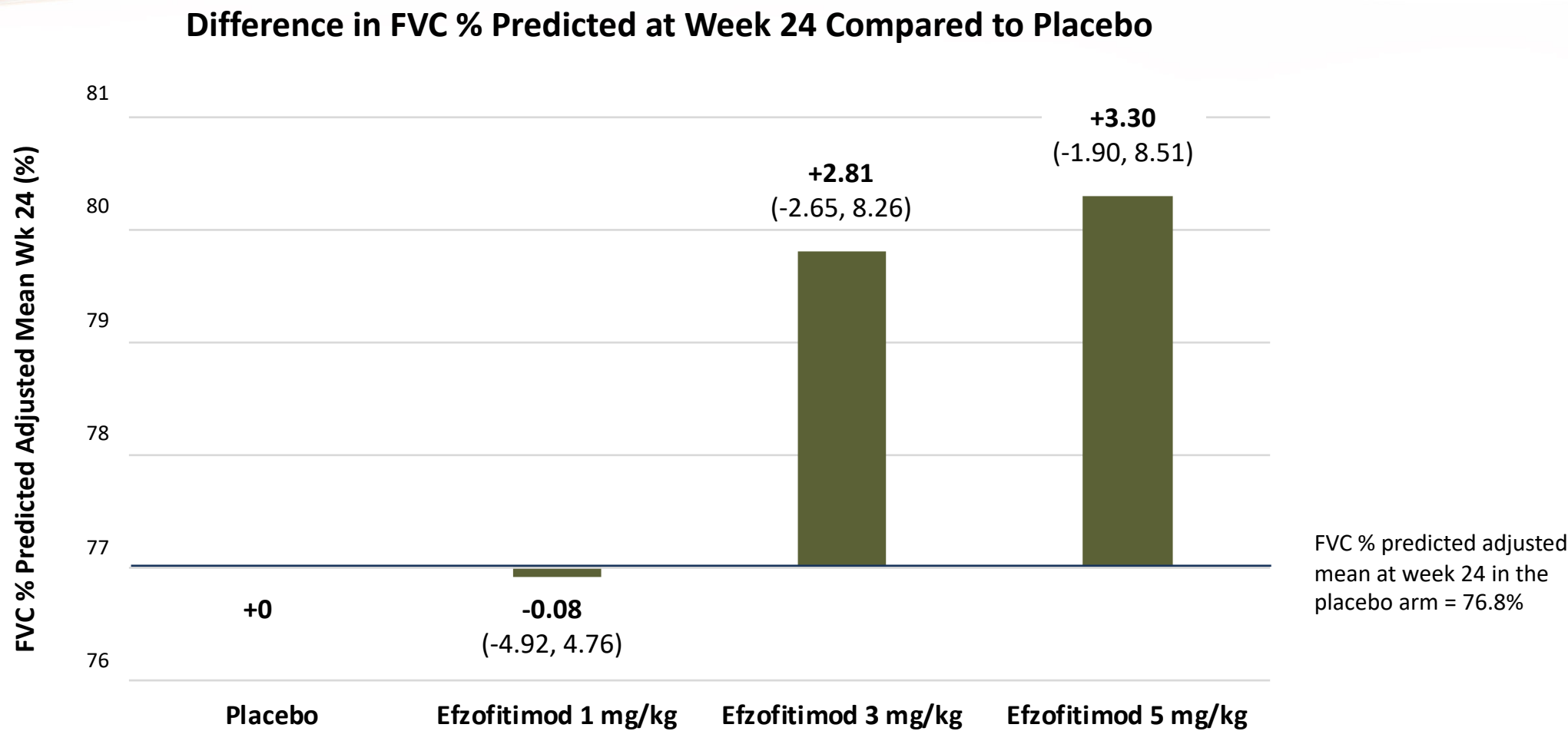
- No new or unexpected findings with repeat dosing
- No dose-response relationship observed
- Most frequent AEs were consistent with underlying disease: Cough, fatigue, wheezing
- No signal of immunogenicity
- No drug related SAEs
- No deaths

Dose-dependent Reduction in Steroid Utilization Compared with Placebo

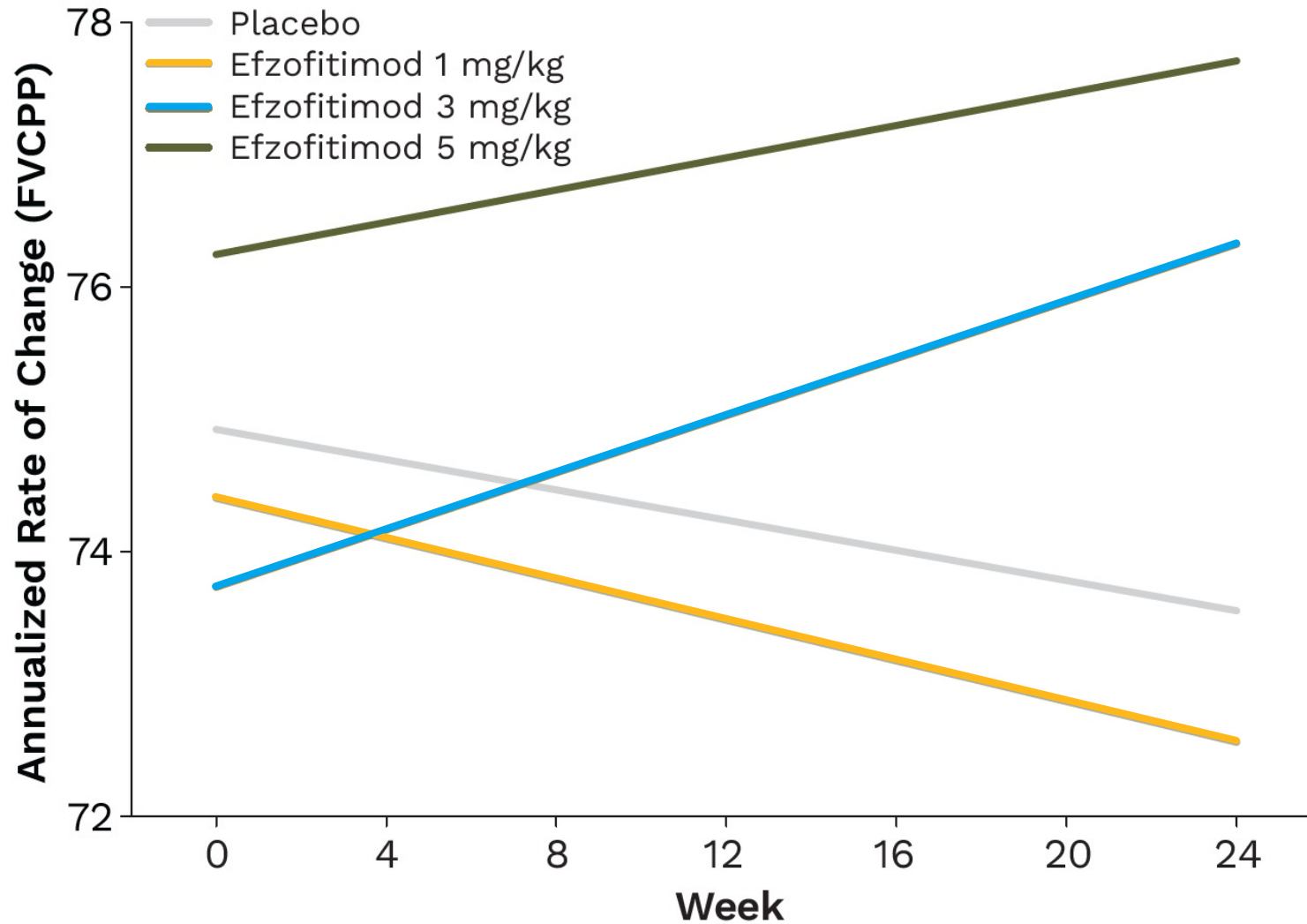
Post-taper Period	Placebo N=12	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 5 mg/kg N=9
Average daily dose (mg), adjusted mean	7.17	6.83	6.54	5.62
- relative reduction vs placebo (%)	-	-5%	-9%	-22%
Change from baseline (%), mean	-46	-41	-49	-58
- difference in adjusted means (%), mean (95% CI)	-	1.2 (-20, 22)	-2.3 (-23, 19)	-12.3 (-33, 8)
Tapered to 0 mg and maintained taper, n (%)	0	0	0	3 (33)

- 58% overall steroid reduction from baseline and 22% relative reduction compared to placebo in steroid utilization post taper in the 5.0 mg/kg treatment group
- 33% of patients able to taper off of steroids completely in 5.0 mg/kg treatment group while controlling disease symptoms

Dose-dependent Improvement in FVC % Predicted Compared to Placebo



Higher Efzofitimod Doses Show Trends of Improvement in FVC % Predicted



Dose-dependent Improvements in PFTs Over Time Compared with Placebo

FVC, mean (SD)	Placebo N=12	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 5 mg/kg N=9
Absolute CFB at Week 24 (mL)	-40 (230)	-80 (160)	120 (130)	110 (250)
FVC % predicted, mean (SD)				
Absolute CFB at Week 24 (%)	-0.9 (6.1)	-2.3 (3.9)	2.6 (2.5)	2.6 (5.6)
DLco % predicted, mean (SD)				
Absolute CFB at Week 24 (%)	-6.2 (14.4)	-6.1 (4.0)	-1.4 (5.0)	4.4 (14.6)

Dose-dependent Clinically Meaningful Symptom Improvements Compared with Placebo

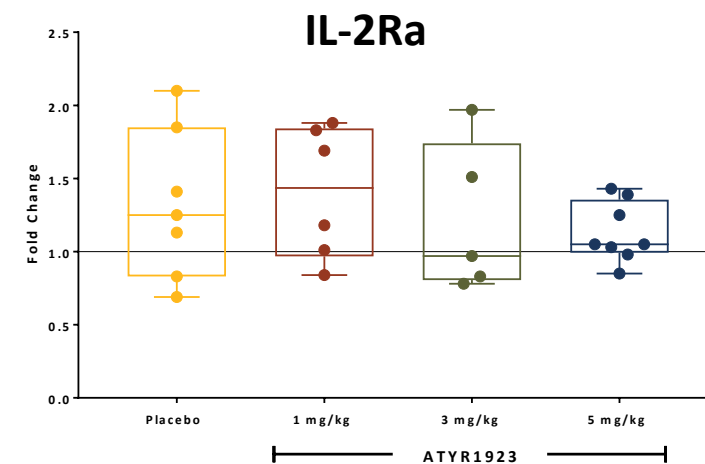
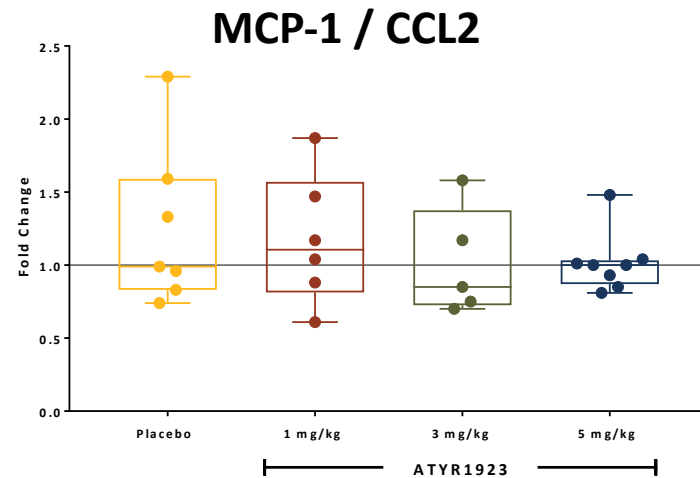
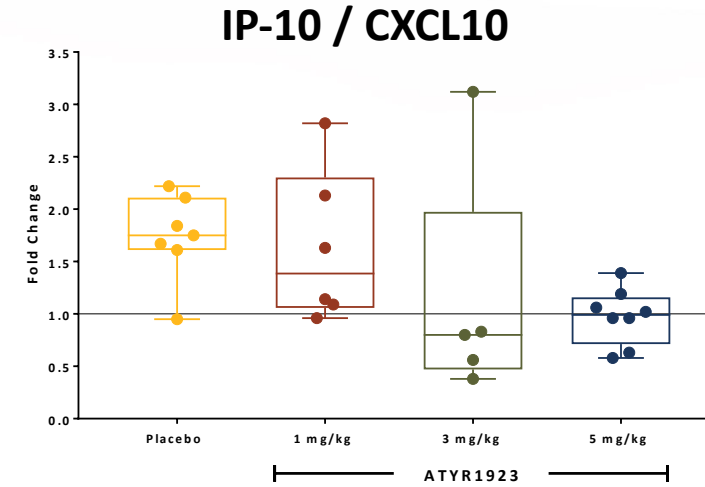
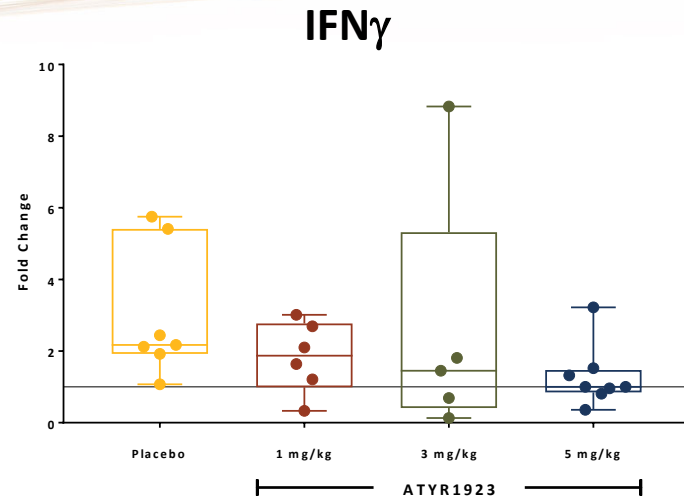
Differences in Adjusted Means vs Pbo at Week 24	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 5 mg/kg N=9
• Dyspnea	-0.76	3.33	4.49
• Cough	-3.49*	2.98*	2.05
• Fatigue	0.76	-4.78	-7.77*
• King's Sarcoidosis Score: Lung	-6.41	11.29	16.17*
• King's Sarcoidosis Score: General Health	-5.1	2.13	18.33*

 = clinically meaningful improvement based on published MCID

*p<0.05 on difference between adjusted means from MMRM; Pbo = Placebo

24 MCIDs: TDI - Witek 2003; LCQ – Raj 2009; FAS - de Kleijin 2011 (Negative score is better for Fatigue); KSQ Lung – Baughman 2021; KSQ Lung – Baughman 2021
TDI: Table 14.2.20.1.1; LCQ: Table 14.2.22.1.1, FAS: Table 14.2.23.1.1, Gen Health: Table 14.2.21.1.1, Lung: Table 14.2.21.1.1

Dose-dependent Control of Key Disease and Inflammatory Biomarkers



Dose Response and Consistent Positive Trends of Efficacy Across all Evaluable Endpoints

- The trial met its primary endpoint: efzofitimod was safe and well-tolerated
- 58% overall steroid reduction from baseline and 22% relative reduction in steroid utilization post taper in the 5.0 mg/kg treatment group
- 33% of patients able to taper completely off steroids in the 5.0 mg/kg treatment group
- 3.3% absolute improvement in lung function as measured by FVC % predicted at week 24 in the 5.0 mg/kg treatment group
- Dose-dependent clinically meaningful improvement in all sarcoidosis symptom measures in the 5.0 mg/kg treatment group
- Dose-dependent improvement on inflammatory biomarkers including IL-6, MCP-1, IFN- γ , IP-10 and TNF α as well as sarcoidosis markers ACE, IL-2Ra and SAA with tightest control in the 5.0 mg/kg treatment group

EFZO-FIT™ : Phase 3 Study of Efzofitimod in Pulmonary Sarcoidosis

Clinical POC Established

- Phase 1b/2a study was first in sarcoidosis to demonstrate effects on physiologic and quality of life measures concurrent with steroid reduction
-

FDA Alignment

- Positive FDA End-of-Phase 2 meeting supports advancement of clinical development
 - Aligned on prioritization of endpoints that are most clinically meaningful to patients and providers
-

Global Pivotal Trial

- Multi-center trial in the U.S., Europe and Japan
 - Multiple sites in the U.S. open for enrollment and actively screening patients
-

Trial Design

Objectives	• Primary: Assess the efficacy of efzofitimod in patients with pulmonary sarcoidosis • Secondary: Assess the safety and tolerability of efzofitimod in patients with pulmonary sarcoidosis • Exploratory: Explore the utility of serum biomarkers in evaluation of interventions to treat pulmonary sarcoidosis
Design	• Phase 3, randomized, double-blind, placebo-controlled, multicenter study
Randomization	• Target enrollment of 264 patients • 1:1:1 efzofitimod 3 mg/kg, efzofitimod 5 mg/kg, or placebo, with 88 patients assigned to each arm • Randomization stratum: ○ Presence or absence of concomitant immunosuppressant therapy, and ○ OCS dose at baseline (< 10 mg/day versus $\geq$ 10 mg/day [prednisone or equivalent])
Duration	• Screening: up to 4 weeks • Treatment Period: 48 weeks (12 monthly doses through Week 44); Primary Assessment at Week 48 • Final Visit: Week 52 (8 weeks post-dose follow-up)

Major Efficacy Endpoints

Primary Endpoint

- Change from baseline in mean daily OCS dose post-taper

Secondary Endpoints

- Annual rate of change in absolute value of FVC
- Percent change from baseline in mean daily OCS dose post-taper at Week 48
- Change from baseline in KSQ-Lung score at Week 48

Key Inclusion / Exclusion Criteria

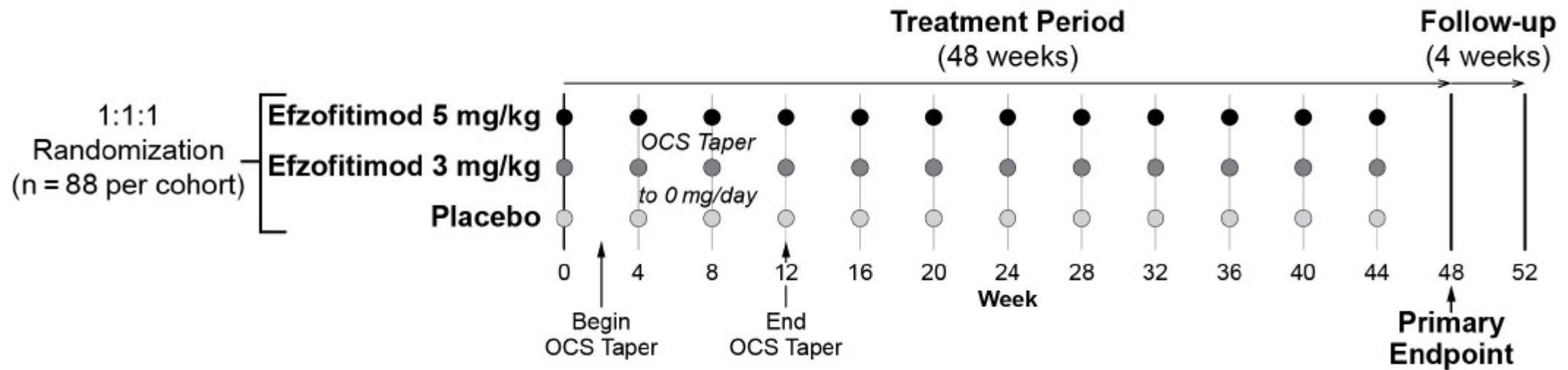
Inclusion

- Adults ages 18-75, inclusive
- Diagnosis of pulmonary sarcoidosis for ≥ 6 months
- Requiring stable treatment with ≥ 7.5 but ≤ 25 mg/day oral corticosteroids
- Medical Research Council (MRC) Dyspnea Scale ≥ 1
- KSQ Lung Score ≤ 70

Exclusion

- Extent of fibrosis $> 20\%$
- Forced Vital Capacity $< 50\%$
- Treatment > 1 oral immunomodulator
- Clinically significant pulmonary hypertension
- Patients with cardiac/neuro/renal sarcoidosis
- Treatment with biological immunomodulators

Phase 3 Study Schema



Multi-center Trial with Sites in the United States, Europe and Japan



Anticipating 60-80 centers in 10 countries



A New Path to Medicine

aTyr: A New Path to Medicine

- Clinically validated platform of proprietary new biology
- Clinical program: efzofitmod (ATYR1923)
 - Novel MOA for fibrotic lung disease
 - Favorable safety profile
 - Proof-of-concept in pulmonary sarcoidosis supports program advancement and expansion to other ILD
 - Orphan drug designation granted for sarcoidosis and systemic sclerosis (scleroderma)
 - Fast Track designation granted for pulmonary sarcoidosis and systemic sclerosis-ILD
 - Recently initiated global pivotal Phase 3 EFZO-FIT™ trial in pulmonary sarcoidosis
- Pipeline in cancer and immunology
 - Lead anti-NRP2 antibody IND candidate for cancer
 - NRP2 antibody research program for distinct therapeutic applications
 - Discovery programs for tRNA synthetases AARS and DARS
- Cash, cash equivalents, and investments at \$89.3m as of June 30, 2022



Thank You