A New Path to Medicine

H.C. Wainwright Global Investment Conference

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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, including efzofitimod and ATYR2810, and development programs, including our NRP2 antibody program and our tRNA synthetase program; 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 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.

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 designation granted
- Positive Phase 1b/2a data for efzofitimod reported Sept. 2021
- Initiation of global pivotal Phase 3 EFZO-FIT™ study expected in Q3 2022

Platform and Target Validation

- Efzofitimod clinical POC validates tRNA synthetase platform and NRP2 as a therapeutic target
- NRP2 antibody ATYR2810 advancing to Phase 1 in 2H 2022
- Future tRNA synthetase discovery work progressing

Financials: Cash, cash equivalents and investments at $98.7m as of March 31, 2022

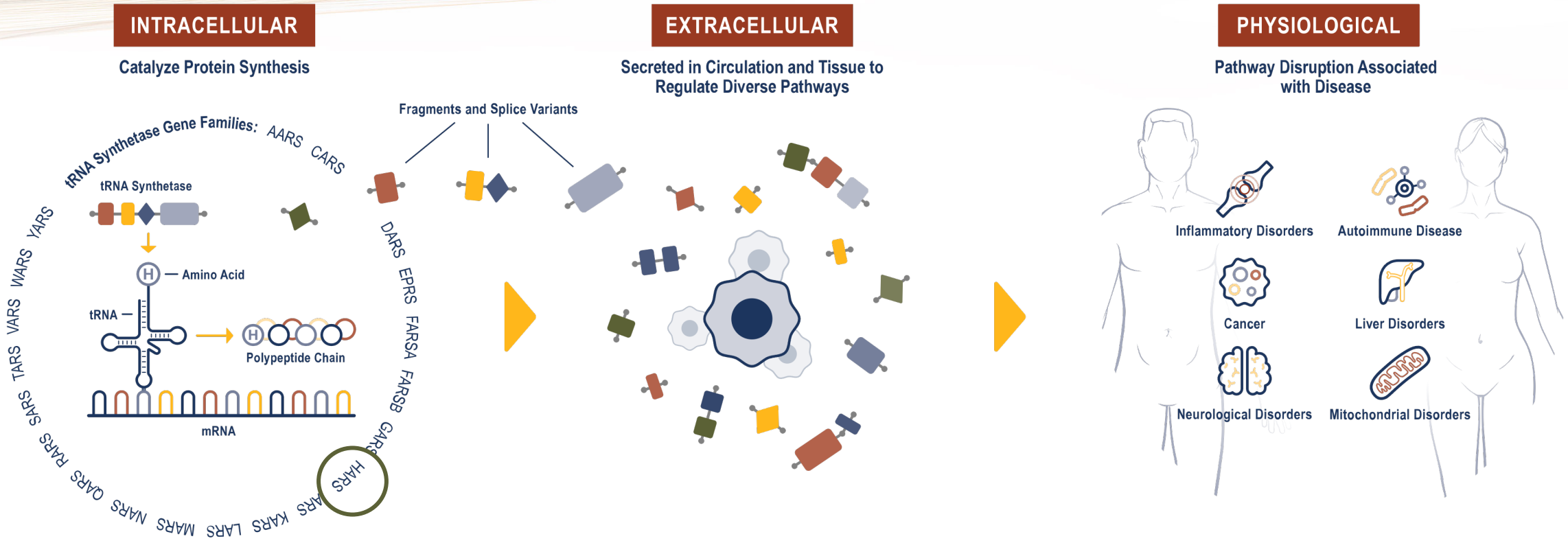
POC – proof-of=concept

aTyr Development Pipeline

PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Efzofitimod (ATYR1923)	Pulmonary Sarcoidosis					
	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

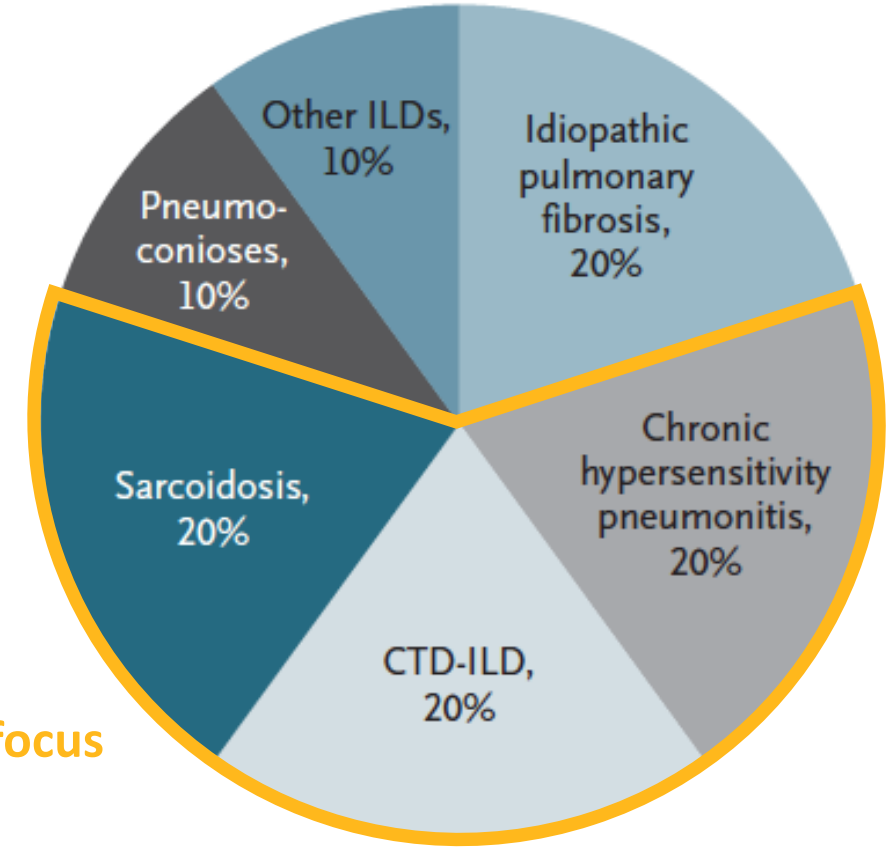
Validated synthetase platform is an engine for new protein therapeutics (e.g. efzofitimod) and new target identification (e.g. NRP2)

Efzofitimod (ATYR1923)

A Novel Immunomodulator for Fibrotic Lung Disease

ILD: A Group of Immune-mediated Fibrotic Lung Diseases

Relative Distribution of ILDs in the USA[1]



aTyr focus

- >200 types of Interstitial Lung Disease (ILD): 4 major types comprise 80% of patients
- IPF is the archetypal fibrotic lung disease, but fibrosis occurs in all types – immune pathology is common to all
- Poor outcomes with limited therapeutic options – immunomodulatory therapy remains SOC outside of IPF
- aTyr focused on 3 main immune-driven types: >500k US patients[2]; ~3m globally
- $2-3b global market opportunity[3]
- Orphan drug designation granted for sarcoidosis and systemic sclerosis (scleroderma)

(1) Lederer, Martinez. NEJM 2018
(2) All ILDs individually have potential for orphan status
(3) aTyr estimates for efzofitimod in Pulmonary Sarcoidosis, CHP, CTD-ILD; excludes IPF

First Efzofitimod Indication: Pulmonary Sarcoidosis

- Multisystem inflammatory disorder of unknown etiology, characterized by the formation of granulomas (clumps of immune cells)
- Lung affected in ~90% of all patients
- ~5x increased mortality in advanced disease
- SOC: corticosteroids; cytotoxic immunosuppressants; anti-TNFs – limited development pipeline
- High unmet need for treatments with improved safety and clinically established efficacy

Large orphan population

50-75% require treatment

Persistent or progressive disease in **30-50%**

10-30% develop fibrosis with **5-10%** mortality

SOC – standard of care; Culver e2019; Baughman 2016; Baughman 2006, Mana 1994; Viskum 1993; Nagai 1999; Judson 1993; Neville 1983; Israel 1986; Wijsenbeek 2019

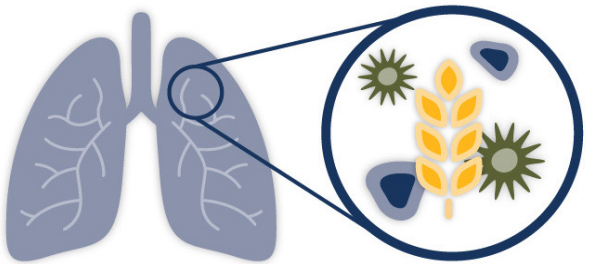
Efzofitimod: Potential First-in-Class Therapy for Immune-Mediated Lung Disease

MOA	• Targets innate and adaptive immune cells during active inflammation to restore immune balance via selective modulation of NRP2
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

MOA = mechanism of action

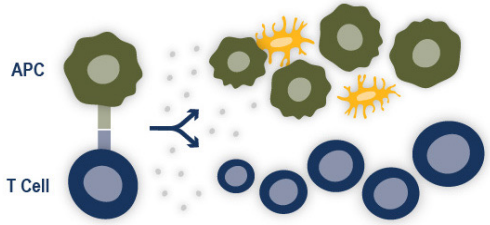
Efzofitimod Therapeutic Goal: Restore Immune Balance and Prevent Fibrosis

Disease Trigger



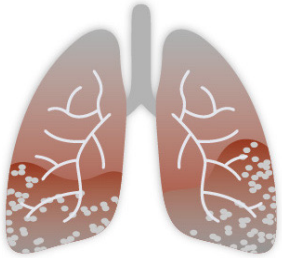
Organic; inorganic; infectious; autoimmune

Aberrant Immune Responses



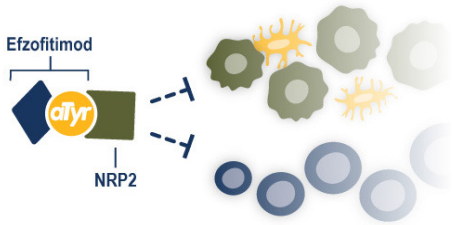
T-cell activation; Pro-inflammatory cytokine/chemokines triggering fibrotic pathways; NRP2 upregulation on immune cells

Lung Inflammation & Fibrosis



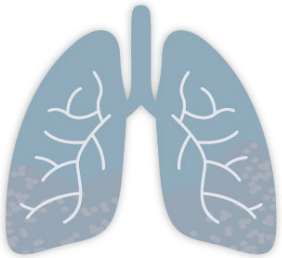
Persistent, unresolved inflammation in the lung can lead to fibrosis; patients experience chronic cough, dyspnea, mortality

Efzofitimod Dampens Immune Responses



Efzofitimod binds to NRP2 and downregulates cytokine and chemokine production and T-cell activation

Stabilized Lung



Reduced inflammation and fibrotic deposition; symptom relief, stabilized lung function*

*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

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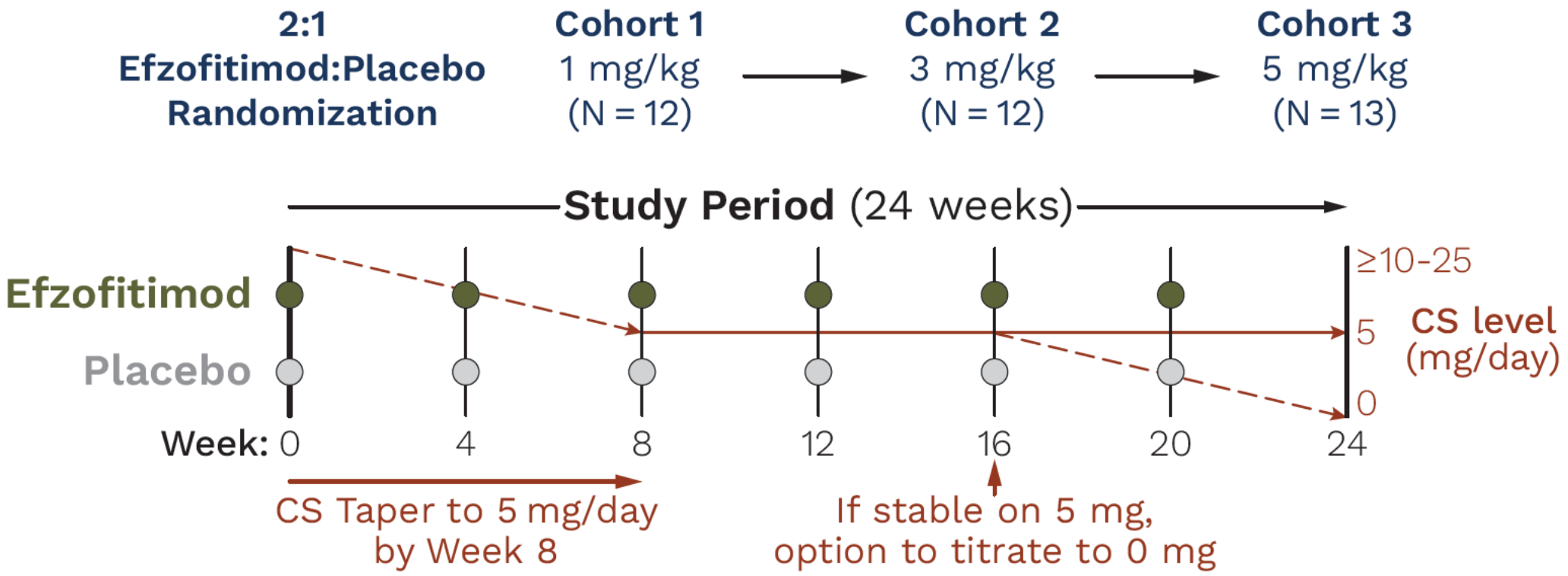
Trial Design

Design	• Randomized (2:1), double-blind, placebo-controlled, multiple ascending dose • 24 week study: 6 monthly IV doses of efzofitimod tested at 1, 3, and 5 mg/kg • Forced steroid taper to 5 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

FVC = Forced Vital Capacity; PFTs = Pulmonary Function Tests

Phase 1b/2a Study Schema



(1) subtherapeutic dose

Baseline Demographics and Disease Characteristics Generally Balanced

Demographics	Placebo N=12	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 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)

Tables 14.1.2.1.1; 14.1.2.2.1; 14.1.2.3.1; 14.1.2.5.1, 14.2.7.1; 14.2.8.1

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

Safety population, Table 14.3.1.1

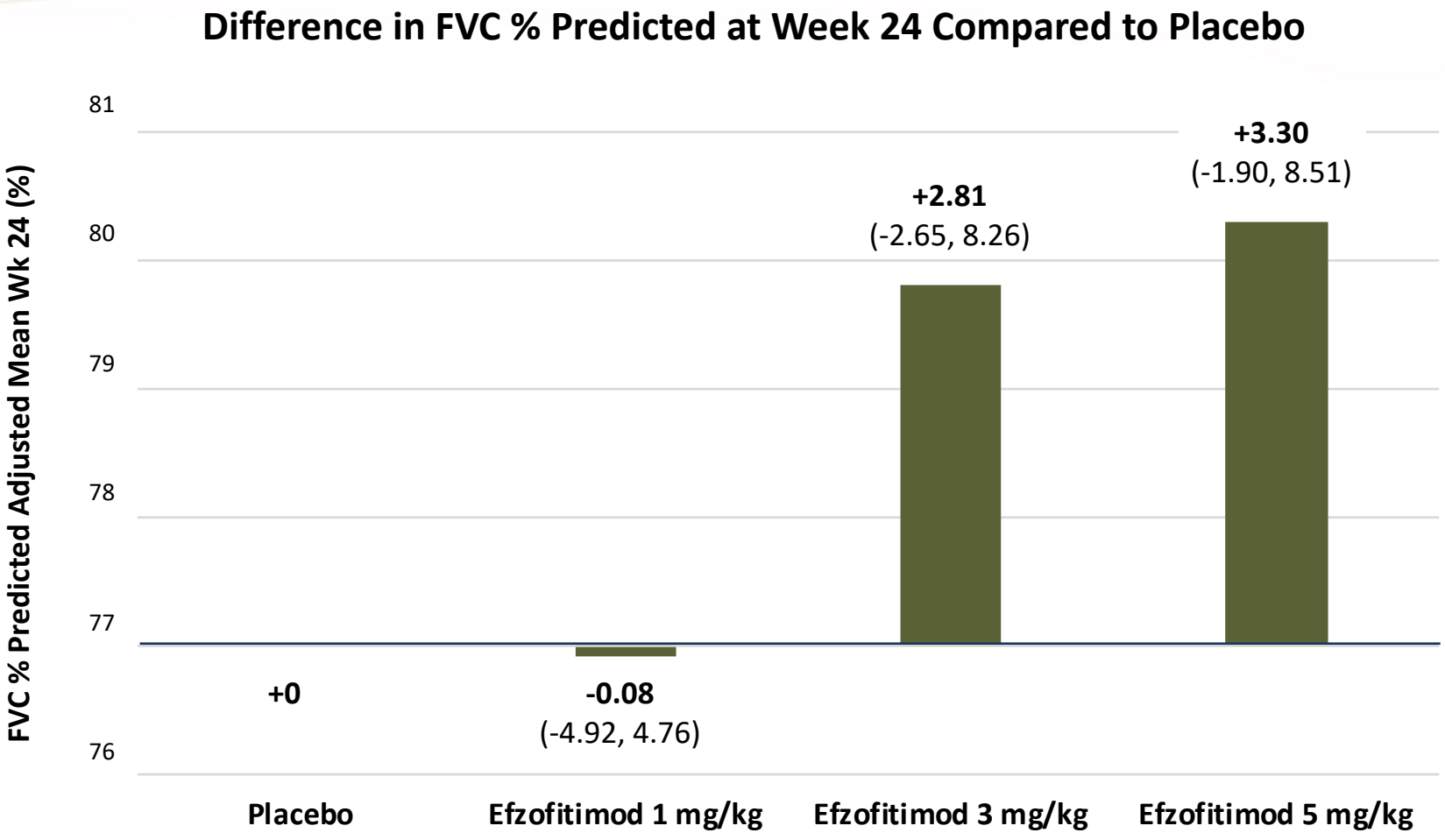
Dose-dependent Reduction in Steroid Utilization Compared with Placebo

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

Table 14.2.1.1.3.1; D51-EOS; adjusted mean refers to least squares mean from ANCOVA adjusting for baseline steroid use

Dose-dependent Improvement in FVC % Predicted Compared to Placebo



FVC % predicted adjusted mean at week 24 in the placebo arm = 76.8%

Table 14.2.8.1; Differences represent from MMRM adjusting for baseline FVC % Predicted, mean (95% CI)

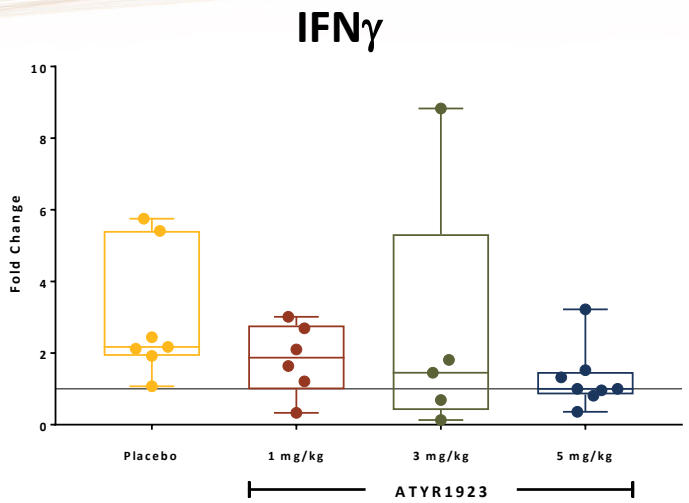
Dose-dependent Clinically Meaningful Symptom Improvements Compared with Placebo

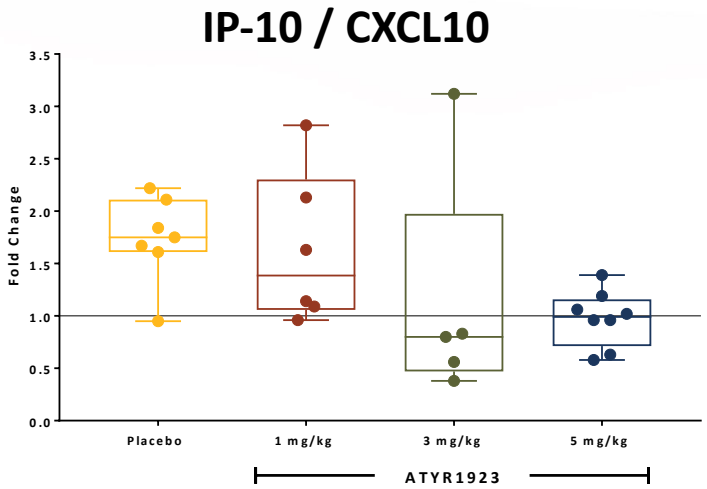
Differences in Adjusted Means vs Pbo at Week 24	Efzofitimod 1 mg/kg N=8	Efzofitimod 3 mg/kg N=8	Efzofitimod 5 mg/kg N=9
• **Dyspnea**	-0.76	3.33	4.49
• **Cough**	-3.49*	2.98*	2.05
• **Fatigue**	0.76	-4.78	-7.77*
• **King's Sarcoidosis Score: Lung**	-6.41	11.29	16.17*
• **King's Sarcoidosis Score: General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

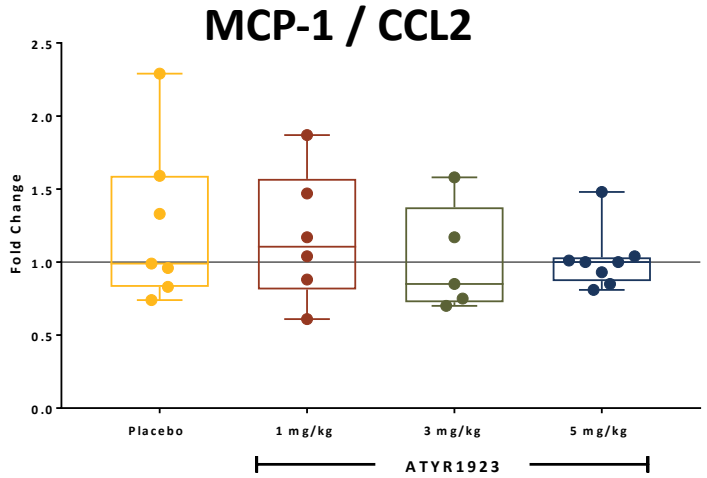
= clinically meaningful improvement based on published MCID

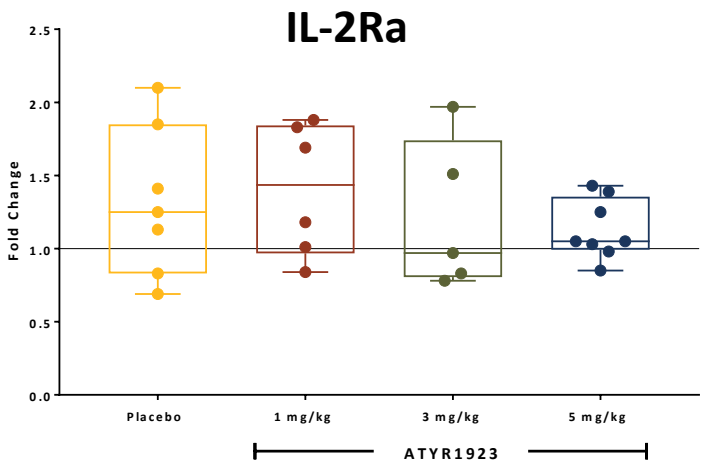
*p<0.05 on difference between adjusted means from MMRM; Pbo = Placebo
MCIDs: TDI - Witek 2003; LCQ – Raj 2009; FAS - de Kleijin 2011 (Negative score is better for Fatigue); KSQ Lung – Baughman 2021; KSQ Lung – Baughman 2021
TDI: Table 14.2.20.1.1; LCQ: Table 14.2.22.1.1, FAS: Table 14.2.23.1.1, Gen Health: Table 14.2.21.1.1, Lung: Table 14.2.21.1.1

Dose-dependent Control of Key Disease and Inflammatory Biomarkers









Graphs represent fold change at Week 24 compared to Baseline

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

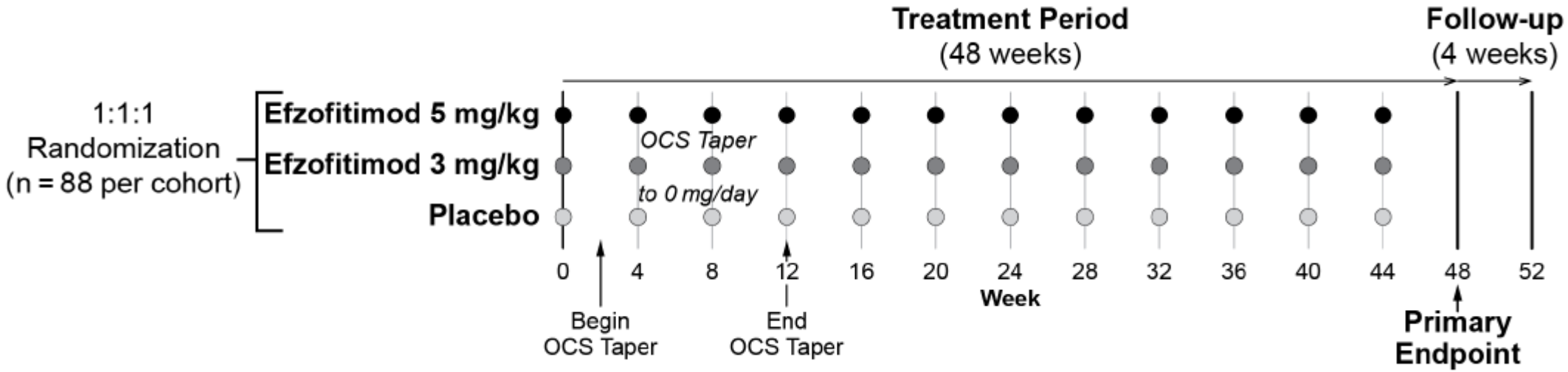
- Multiple sites in North America, Europe and Japan
- Expected to initiate in Q3 2022

aTyr

Trial Design

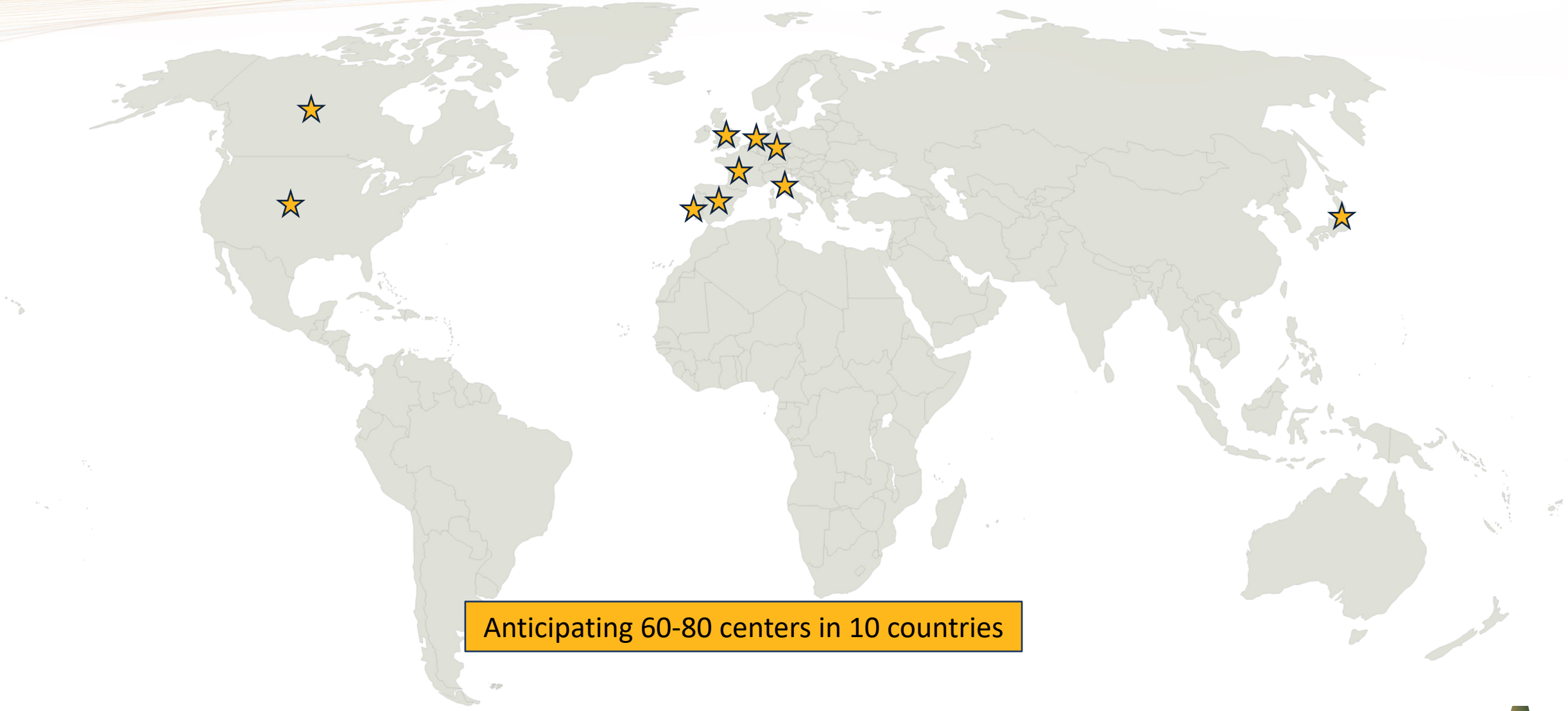
Objectives	• Primary: Assess the efficacy of efzofitimod in patients with pulmonary sarcoidosis • Secondary: Assess the safety and tolerability of efzofitimod in patients with pulmonary sarcoidosis • Exploratory: Explore the utility of serum biomarkers in evaluation of interventions to treat pulmonary sarcoidosis
Design	• Phase 3, randomized, double-blind, placebo-controlled, multicenter study • 1:1:1 efzofitimod 3 mg/kg, efzofitimod 5 mg/kg, or placebo, with 88 patients assigned to each arm • Forced steroid taper to 0mg by week 12
Population	• 264 pulmonary sarcoidosis patients with diagnosis of disease for ≥6 months • ≥7.5 but ≤25 mg/day stable oral corticosteroid treatment • Symptomatic/active disease at baseline
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)
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

Phase 3 Study Schema



OCS = oral corticosteroids

Multi-center Trial with Sites in North America, Europe and Japan



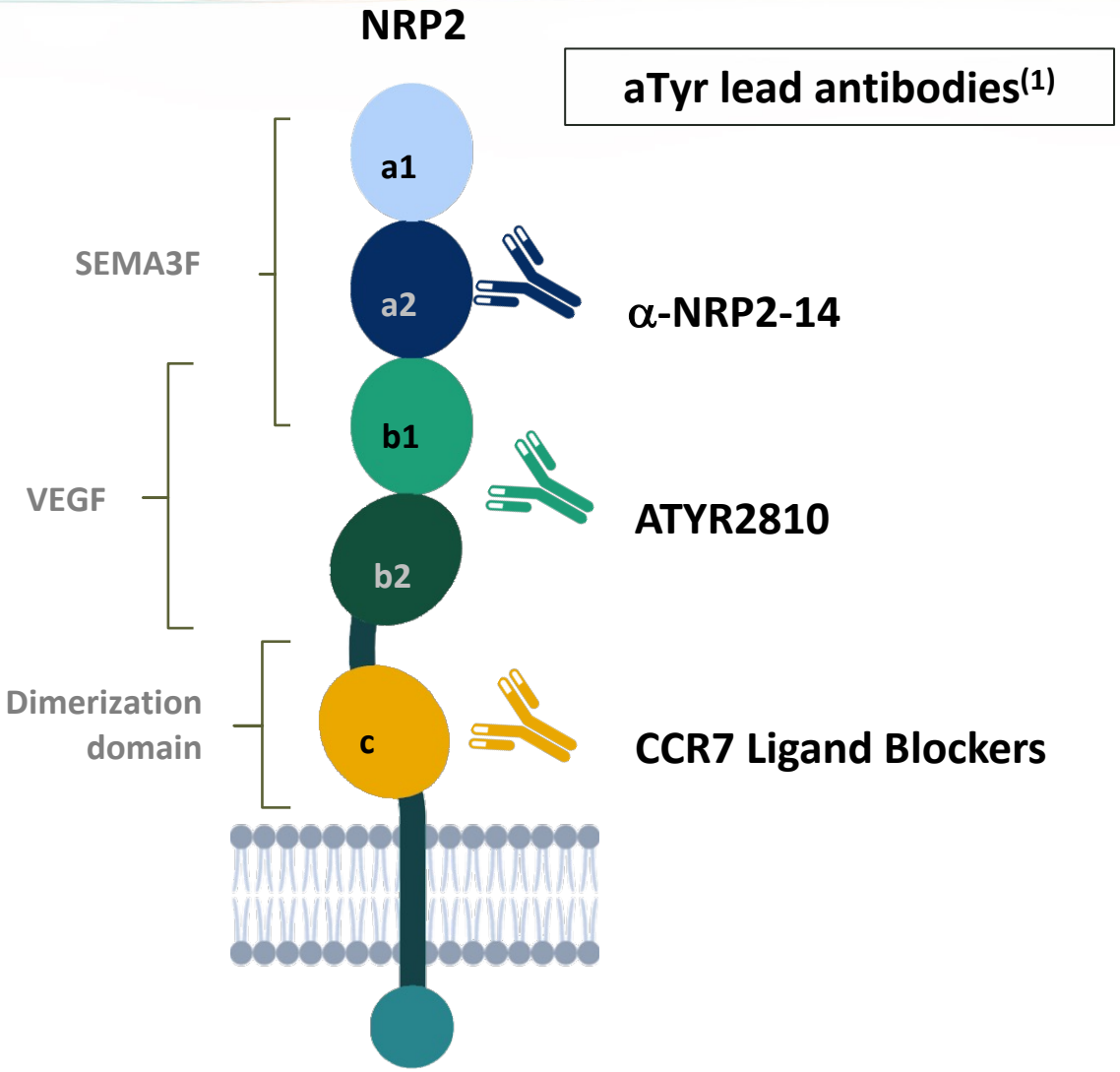
Anticipating 60-80 centers in 10 countries

NRP2 Antibodies

Regulating Diverse Disease Pathways

NRP2: A Novel Therapeutic Target

- NRP2 is a potentially novel drug target for cancer and inflammatory disorders
- Acts as a co-receptor for VEGF, semaphorins and certain chemokines (e.g., CCL21)
- Highly expressed on certain solid tumors (e.g. breast, lung, renal); expression is associated with worse outcomes in many cancers
- aTyr mAbs selectively target distinct epitopes for differentiated therapeutic applications
- Superior specificity and sensitivity compared to commercially available antibodies in preclinical studies



(1) Distinct from efzofitimod interaction with NRP2

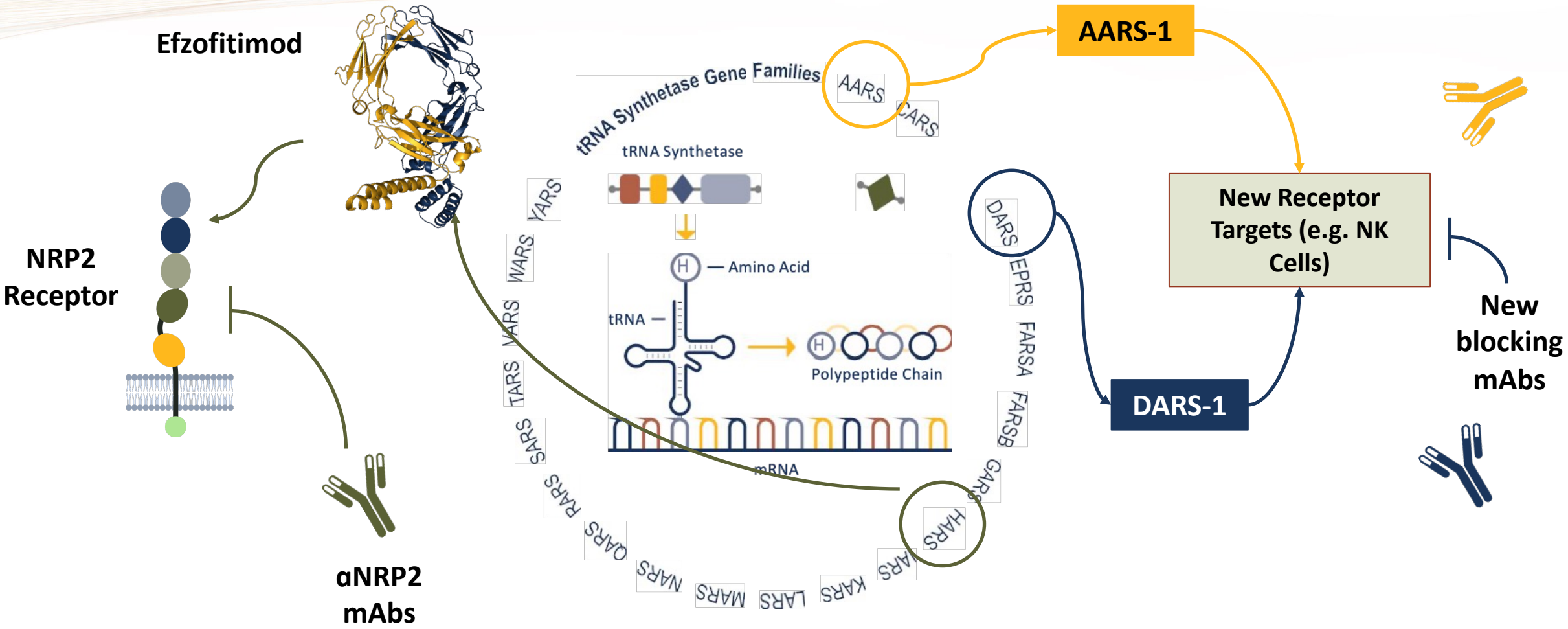
ATYR2810: Lead Anti-Neuropilin-2 Antibody IND Candidate for Cancer

- Fully humanized mAb that specifically and functionally blocks the interaction between NRP2 and VEGF
- VEGF is a validated mediator of tumor survival and growth and plays a role in tumor invasiveness and metastasis
- Current therapies that directly target VEGF / VEGF-R do not block binding to NRP2
- Blocking the NRP2 / VEGF interaction is a differentiated approach to reduce metastasis and chemoresistance through inhibition of key regulators of lineage plasticity, such as epithelial-mesenchymal transition (EMT)
- Preclinical data suggest that ATYR2810 may be an effective novel therapeutic antibody that can target aggressive cancers through inhibition of key regulators of lineage plasticity, inhibition of metastasis, and enhanced chemosensitivity
- Plan to initiate clinical trial in patients in 2H 2022

tRNA Synthetases

A Potential New Therapeutic Protein Class

tRNA Synthetase Engine



aTyr owns IP covering all 20 tRNA synthetase gene families

aTyr

A New Path to Medicine

aTyr: A New Path to Medicine

- Clinically validated platform of proprietary new biology
- Clinical program: efzofitimod (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)
  - Initiation of global pivotal Phase 3 EFZO-FIT™ trial in pulmonary sarcoidosis in Q3 2022
- 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 initially focusing on NK cell biology
- Cash, cash equivalents, and investments at $98.7m as of March 31, 2022

Future Milestones

Efzofitimod (ATYR1923)	• Publication of Phase 1b/2a results in pulmonary sarcoidosis patients • Initiation of global pivotal Phase 3 EFZO-FIT™ trial in pulmonary sarcoidosis patients expected in Q3 2022 • Phase 2 ready for initiation of trials in other ILD
ATYR2810	• Initiation of Phase 1 clinical trial expected in 2H 2022
Discovery pipeline	• New NRP2 mAb opportunities targeting distinct NRP2 epitopes • Advance AARS and DARS derived product candidates

aTyr

Thank You