Translating New Immune Pathways into Meaningful Medicines

Biotech Showcase

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aTyr Pharma

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Accelerating Value Creation from Novel Biology

Platform of New Biology:

Discovery pipeline of novel therapeutic candidates based on proprietary knowledge of extracellular functions of tRNA synthetases (~300 protein compositions patented)

Lead Product Candidate: ATYR1923

Engineered, long acting, protein therapeutic, derived from the HARS gene, for the treatment of pulmonary sarcoidosis

Financials:

Cash, cash equivalents and investments at
$56.0m as of 9/30/2018

Clinical Milestones:

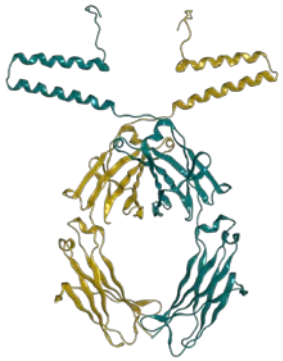
- ✓ Initiated P1b/2a Trial – 4Q 2018
- ❑ Interim Results – 4Q 2019*
- ❑ Final Results – mid-2020*

* *Dependent on patient enrollment*

Extracellular tRNA Synthetase Biology Associated with Disease in Multiple Tissues

tRNA Synthetase Gene Families

AARS	**HARS**	RARS
CARS	IARS	SARS
DARS	KARS	TARS
EPRS	LARS	VARS
FARS	MARS	WARS
FARSB	NARS	YARS
GARS	QARS	



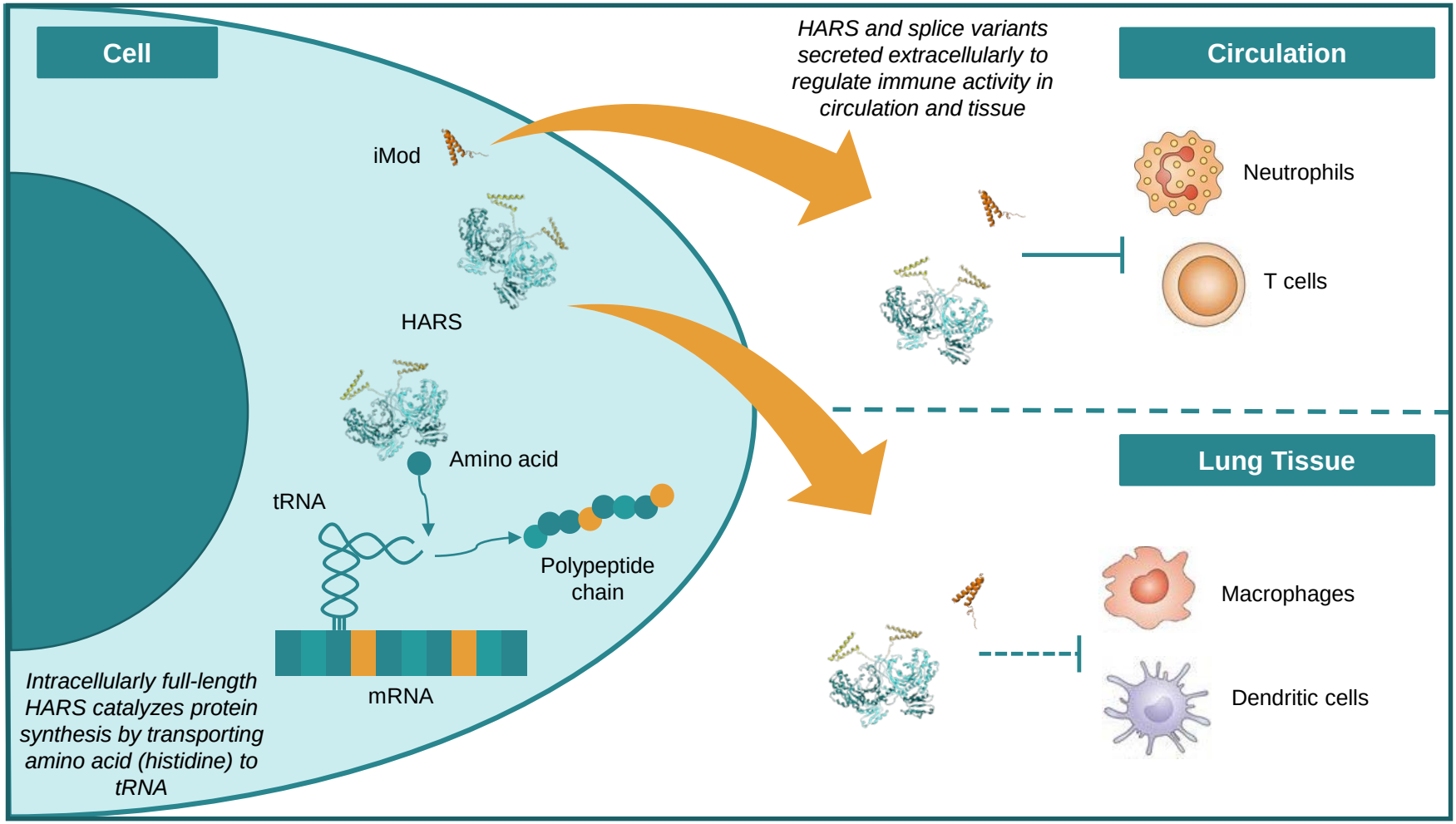
Drugs: ATYR1923
Function: Immuno-modulatory
Disease: Interstitial Lung Disease

aTyr's current R&D focus

Known disease connections:
- Cancer
- Autoimmune disease
- Liver disorders
- Inflammatory disorders
- Neurological disorders
- Mitochondrial disorders

Pipeline opportunities

Novel tRNA Synthetase Domains Secreted Extracellularly with Non-Catalytic Functions

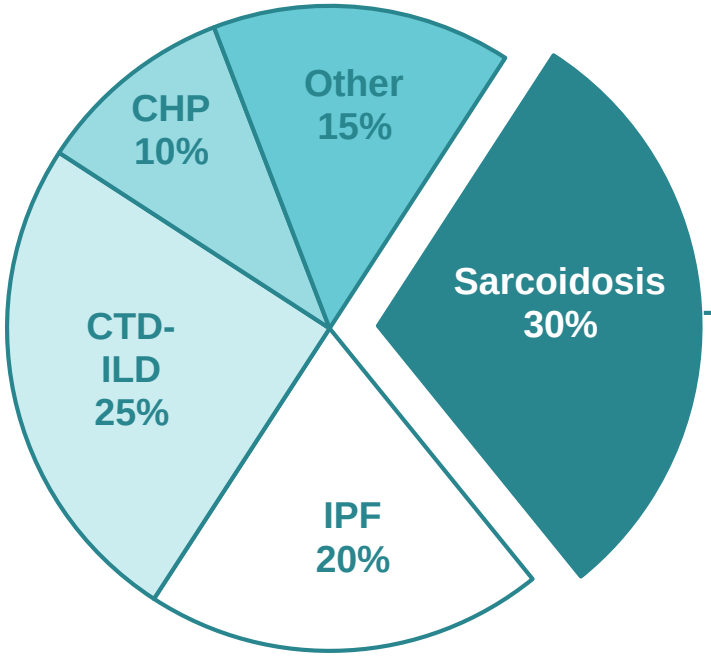


ATYR1923

For the Treatment of Pulmonary Sarcoidosis

Sarcoidosis: The Most Common Form of Interstitial Lung Disease

Interstitial Lung Diseases



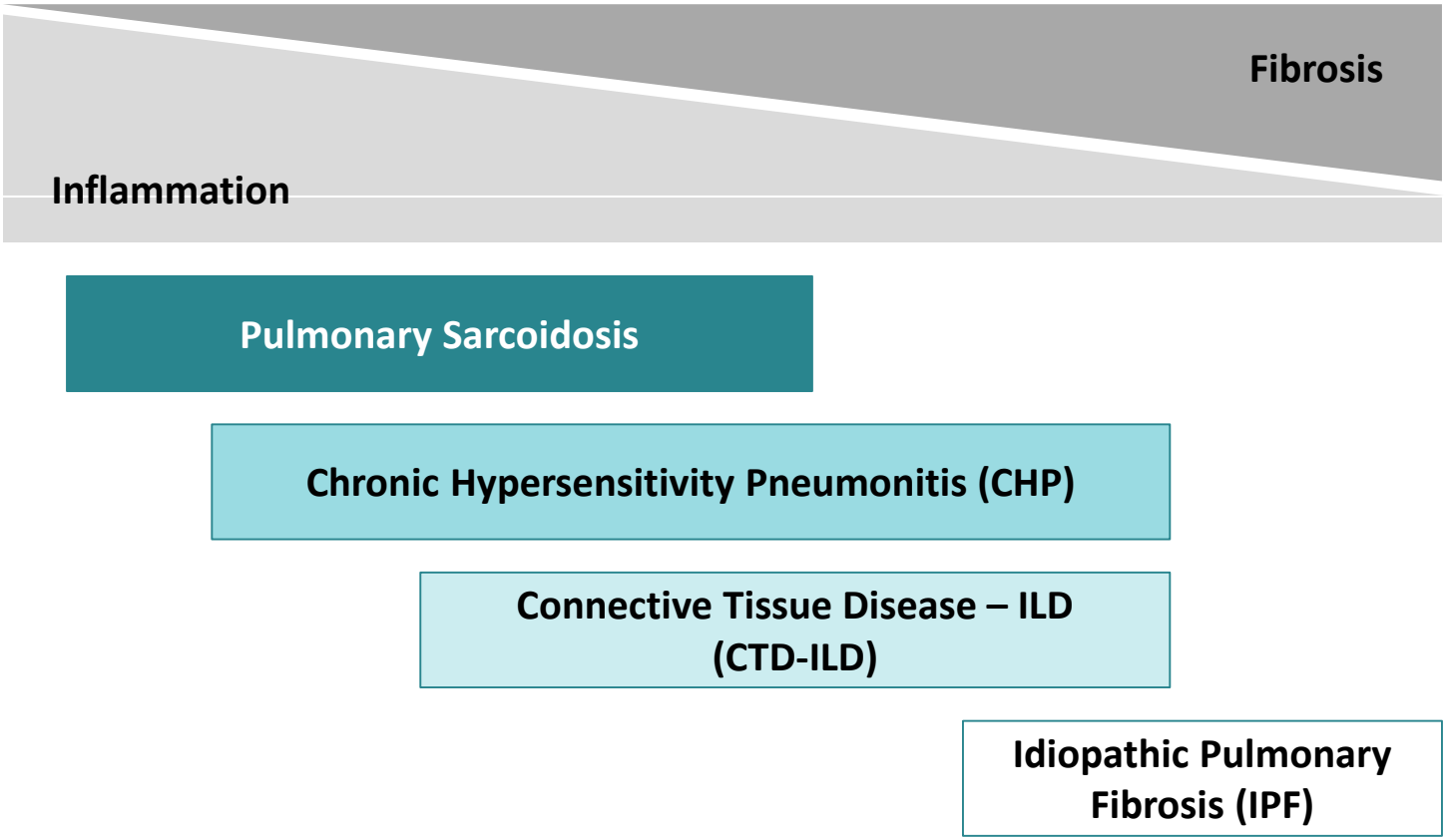
$2-3B Global Opportunity

50% require systemic therapy

30% with chronic progressive disease despite currently available treatment

IPF: Idiopathic Pulmonary Fibrosis; CHP: Chronic Hypersensitivity Pneumonitis; CTD-ILD: Connective Tissue Disease Associated ILD

Interstitial Lung Diseases Share Persistent Immune Engagement



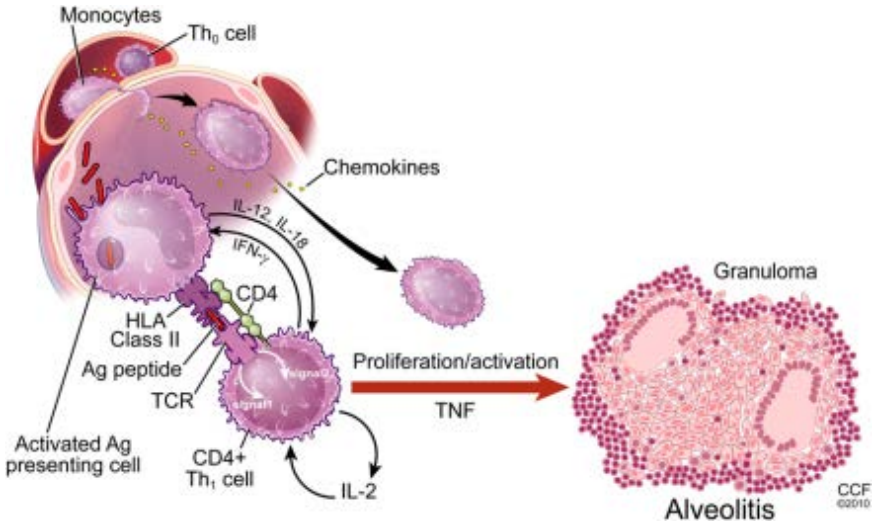
Slide adapted from Dr. Steven Nathan, Medical Director, Advanced Lung Disease and Transplant Program at Inova Fairfax Hospital, Falls Church, VA

First-in-Patient Population: Pulmonary Sarcoidosis

- Systemic inflammatory disorder characterized by the formation of granulomas (clumps of inflammatory cells) in one or more organs of the body
- CD4+ (Th1 / Th17) T-cell driven
- Usually begins in the lungs, skin or lymph nodes
- Sarcoidosis in the lungs is called pulmonary sarcoidosis and occurs in ~90% of patients

Unmet needs[1]:

- Better understanding of pathogenesis
- Prognostic stratification and targeted management
- Better therapies, with quicker onset of action and less toxicity

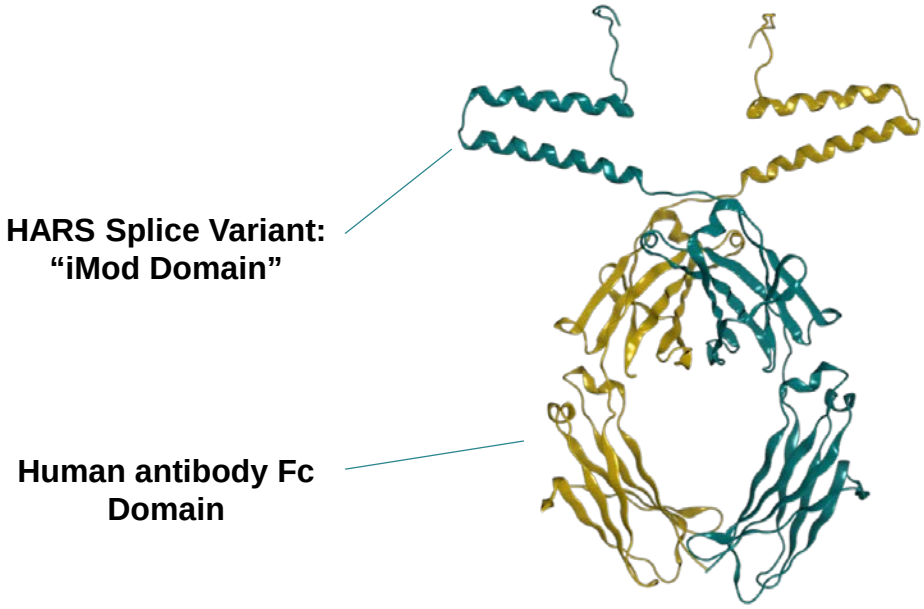


Baughman RP, Culver DA, Judson MA. AM J Respir Crit Care Med 2011

[1]Dan Culver, Cleveland Clinic

ATYR1923: Novel Engineered Protein Therapeutic

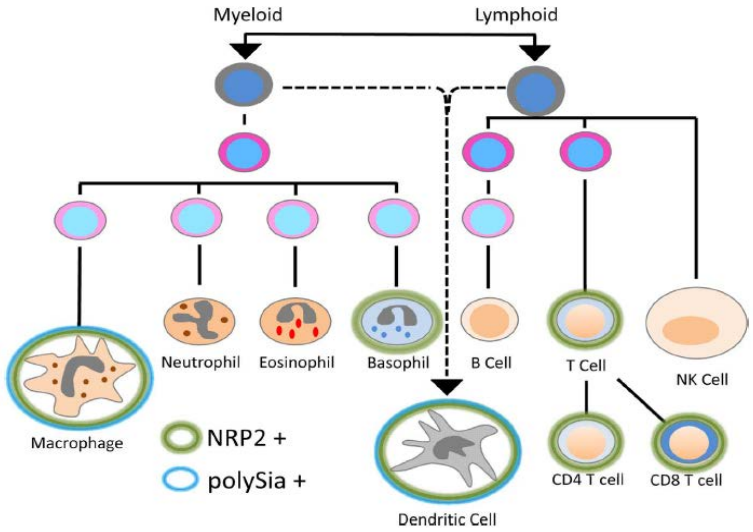
- Active domain (iMod) is naturally occurring splice-variant of HARS that is enriched in the human lung
- Binds selectively to Neuropilin-2 (NRP2)
- Regulates a number of immune cell-types, including: T cells, Neutrophils, Macrophages, Dendritic cells



Receptor: Importance of NRP-2 as a Binding Partner for ATYR1923

- Pleiotropic receptor that can bind to a number of different ligands
- Well-established role in the development of the neural and lymphatic systems
- Emerging role in the immune system; present on a number of immune cell types
- Expressed on alveolar macrophages; may play role in regulating lung inflammation (1)

Immune cells where NRP-2 is expressed (2)



(1) Immormino et al. *Neuropilin-2 regulates airway inflammatory responses to inhaled lipopolysaccharide.* Am J Physiol Lung Cell Mol Physiol 315: L202-L211. 2018.

(2) Schellenberg et al. *Role of Neuropilin-2 in the immune system.* Mol. Immunol. 90, 239-244, 2017

Pre-Clinical Translational Estate Supports Clinical Development in ILD

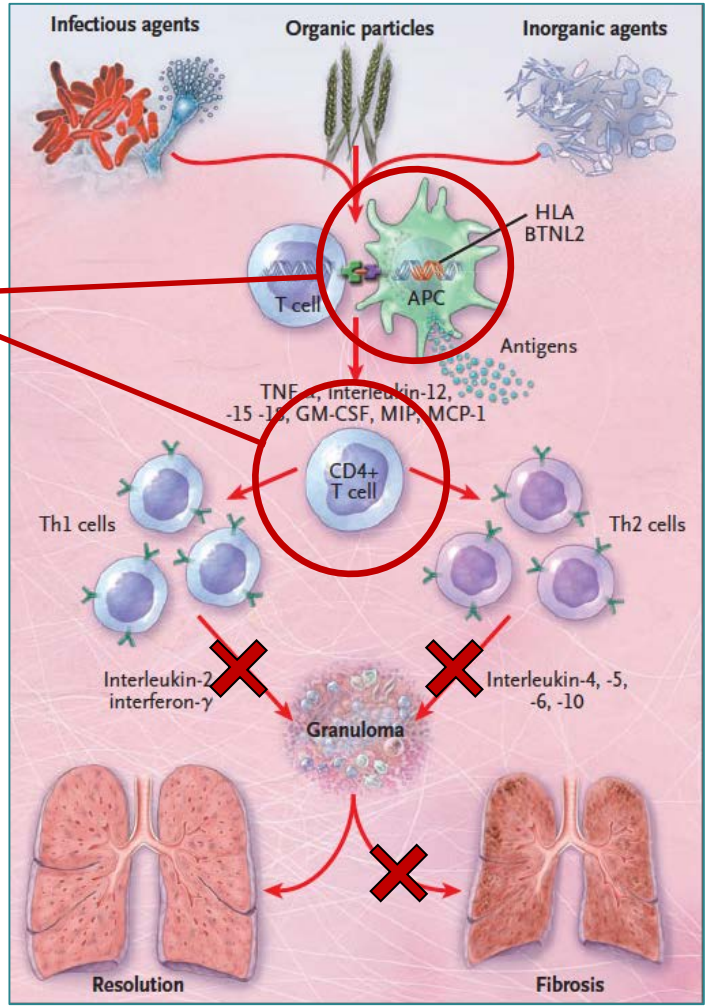
Bleomycin-Induced Lung Injury (Mouse)	• ATYR1923 vs. pirfenidone* • ATYR1923 reduced fibrosis and inflammation • Presented at ATS, May 2017
Bleomycin-Induced Lung Injury (Rat)	• ATYR1923 vs. nintedanib** • ATYR1923 returned lung function to normal and reduced fibrosis and inflammation • Presented at ATS, May 2018
Sclerodermatous chronic-graft vs host disease (Mouse)	• ATYR1923 vs. nintedanib** • ATYR1923 reduced lung and skin fibrosis • Presented at Scleroderma Foundation Patient Conference, July 2018

*2017 annual sales of Esbriet® (pirfenidone) ~869M CHF, 13% increase YoY

**2017 annual sales of Ofev® (nintedanib) ~920M Euros, 52.3% increase YoY

ATYR1923 Intervention in Pulmonary Sarcoidosis

ATYR1923 Therapeutic Hypothesis:
Downregulate inflammatory insult and prevent progression to fibrosis

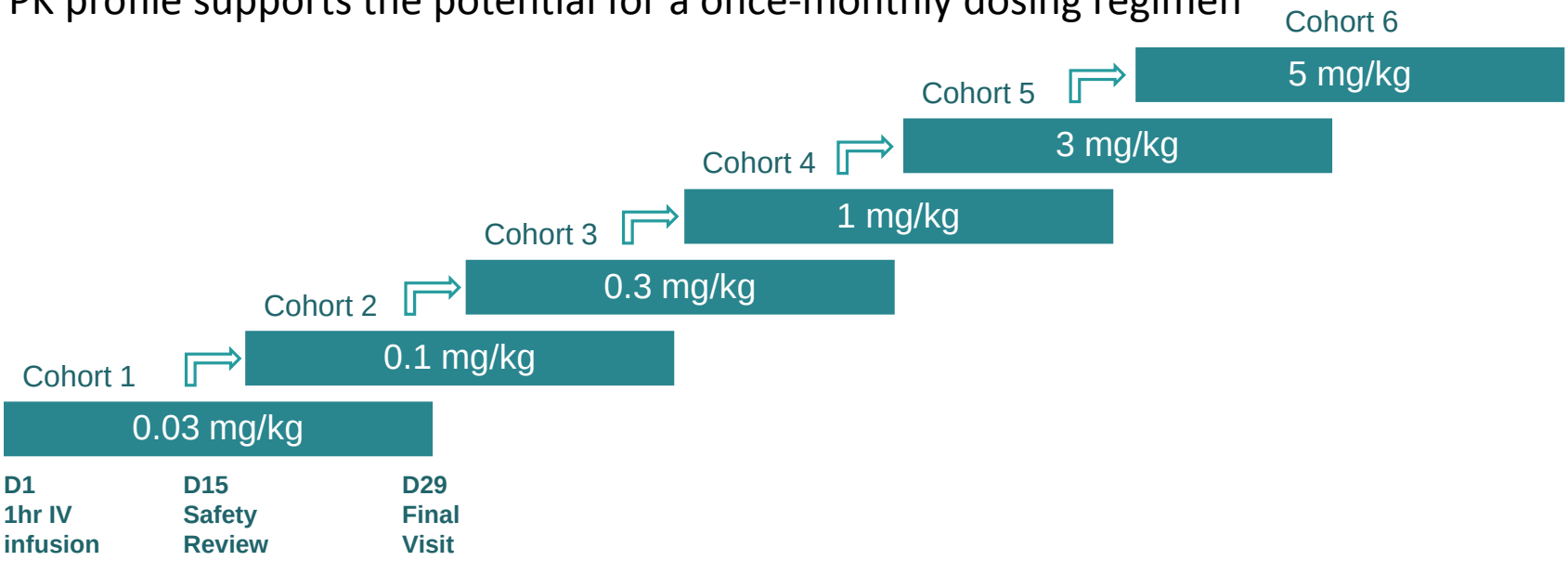


Hypothesized Immunopathogenesis of Sarcoidosis adapted from Iannuzzi et al, NEJM, 2007

Phase 1 Healthy Volunteer Study Completed

Positive Phase 1 Data Announced in June 2018

- Randomized, double-blind, placebo-controlled, single ascending dose (N=36 HVs)
- ATYR1923 was generally well-tolerated with no significant adverse events
- PK profile supports the potential for a once-monthly dosing regimen



ATYR1923 Phase 1b/2a Study in Pulmonary Sarcoidosis

Objectives	• Evaluate safety, tolerability, PK, and immunogenicity of multiple ascending doses of ATYR1923 • Evaluate signals of drug activity through steroid dose reduction and FDG-PET/CT changes
Design	• Randomized, double-blind, placebo-controlled, multiple ascending dose
Population	• Histologically confirmed pulmonary sarcoidosis • Requiring ≥10 mg prednisone (steroid) treatment; capable of steroid taper • Symptomatic/active disease at baseline by ^{18F}-FDG-PET/CT, Pulmonary Function Tests
Dosing	• 3 sequential cohorts, 12 patients each • 2:1 randomization • ATYR1923 doses: 1.0, 3.0, and 5.0 mg/kg
Duration	24-week study period • Steroid taper phase down to 5 mg by week 8 • 16-week maintenance phase
Sites	• Up to 12 leading pulmonary sarcoidosis centers in US • Collaboration with the Foundation for Sarcoidosis Research

ATYR1923 Phase 1b/2a Study Endpoints

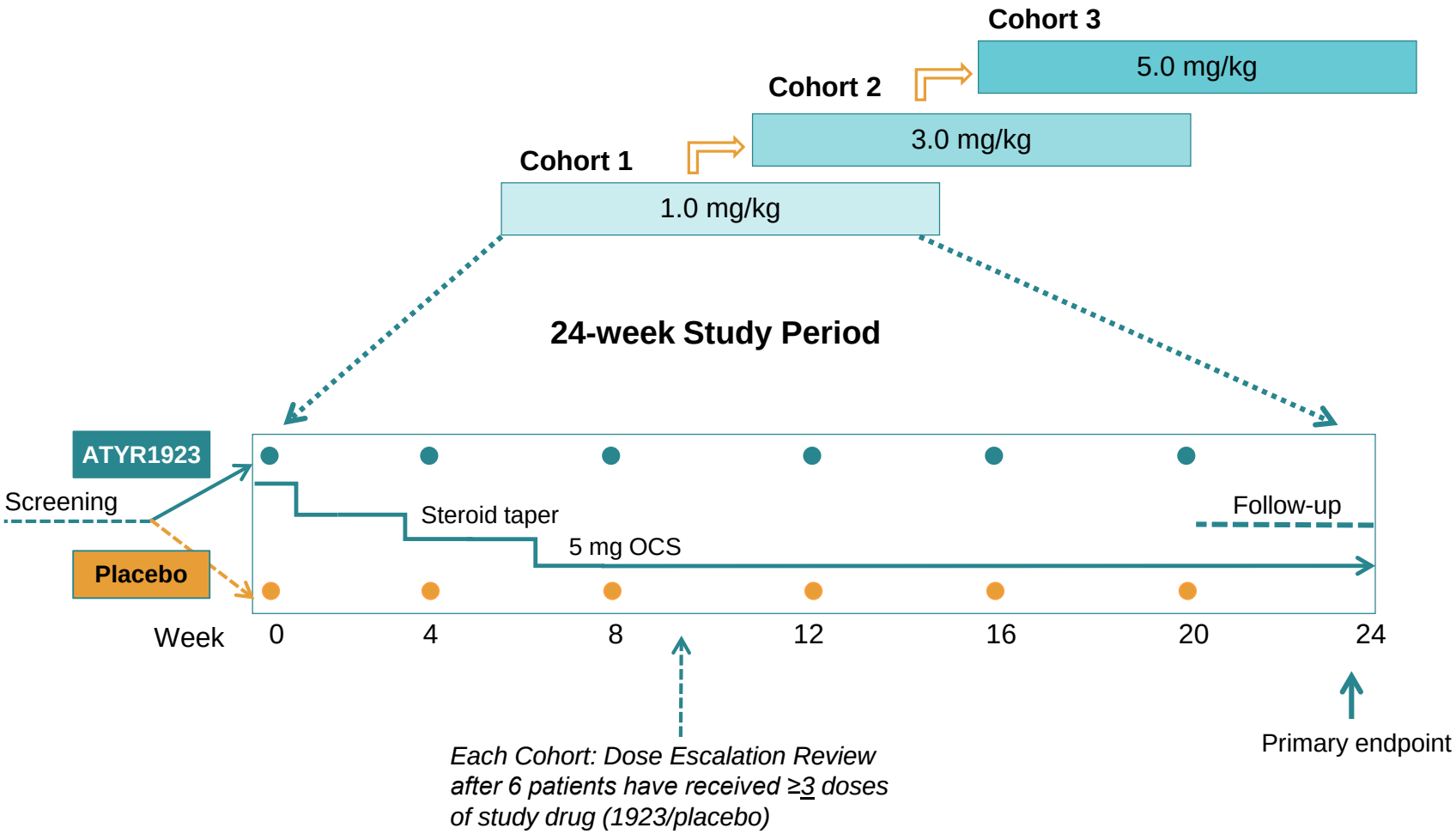
Primary

- Safety and tolerability of multiple ascending IV ATYR1923 doses

Secondary

- Steroid-sparing effect
- Immunogenicity
- Pharmacokinetics (PK)
- Exploratory efficacy measures: FDG-PET/CT imaging; Lung function (FVC); Serum biomarkers; Health-related quality of life scales

ATYR1923 Phase 1b/2a Study Schema



ATYR1923 Phase 1b/2a Study in Pulmonary Sarcoidosis Initiated

Status	• US IND accepted • Up to 12 leading Pulmonary Sarcoidosis centers in US • Site initiation activities ongoing
Timelines*	• Interim data: 4Q 2019 • Study completion: mid-2020
Possible Future Development	• Registrational trial in Pulmonary Sarcoidosis • Initiate P2 studies in other types of interstitial lung disease (e.g. CTD-ILD; CHP)

*Dependent on patient enrolment

Mission: Generate Value for Patients and Shareholders

- ✓ aTyr owns IP estate directed to a potential pipeline of proteins derived from 20 tRNA synthetase genes
- ✓ ATYR1923 *in-vitro* and *in-vivo* studies support clinical development in ILD
- ✓ Identification of NRP-2 receptor for ATYR1923 elucidates greater understanding of MOA
- ✓ Positive Phase 1 data for ATYR1923
- ✓ Initiated Phase 1b/2a study of ATYR1923 in patients with pulmonary sarcoidosis
- ❑ Goal is to demonstrate safety and preliminary clinical activity in ATYR1923 pulmonary sarcoidosis trial
- ❑ Potential to expand into other ILD indications

Thank You