

Translating New Immune Pathways into Meaningful Medicines

The Cowen & Co. 39th Annual Health Care Conference 2019

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We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this presentation are the property of their respective owners. Solely for convenience, the trademarks and trade names in this presentation are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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 and other interstitial lung diseases

\$2-3b⁽¹⁾ global opportunity

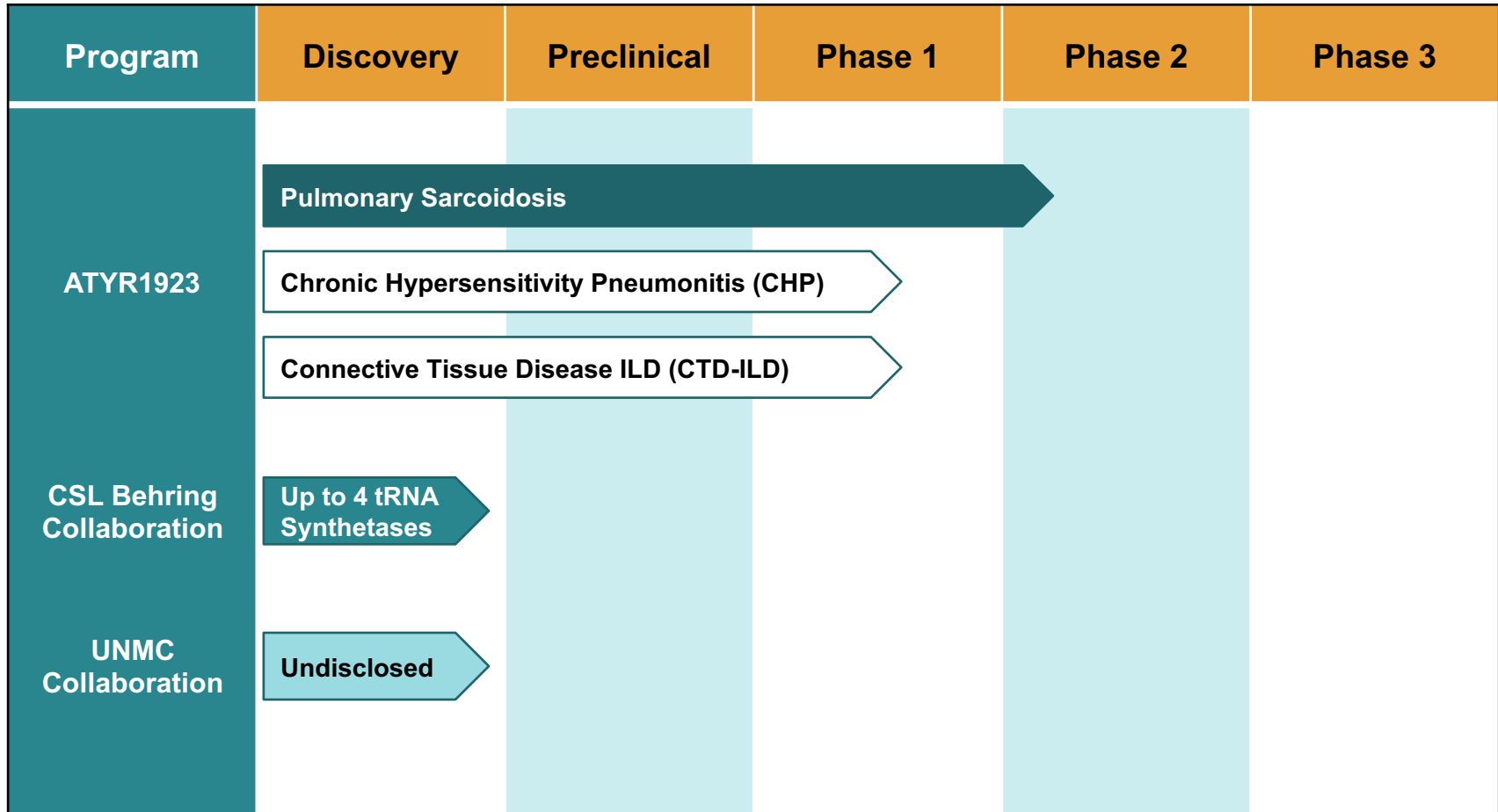
Financials:

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

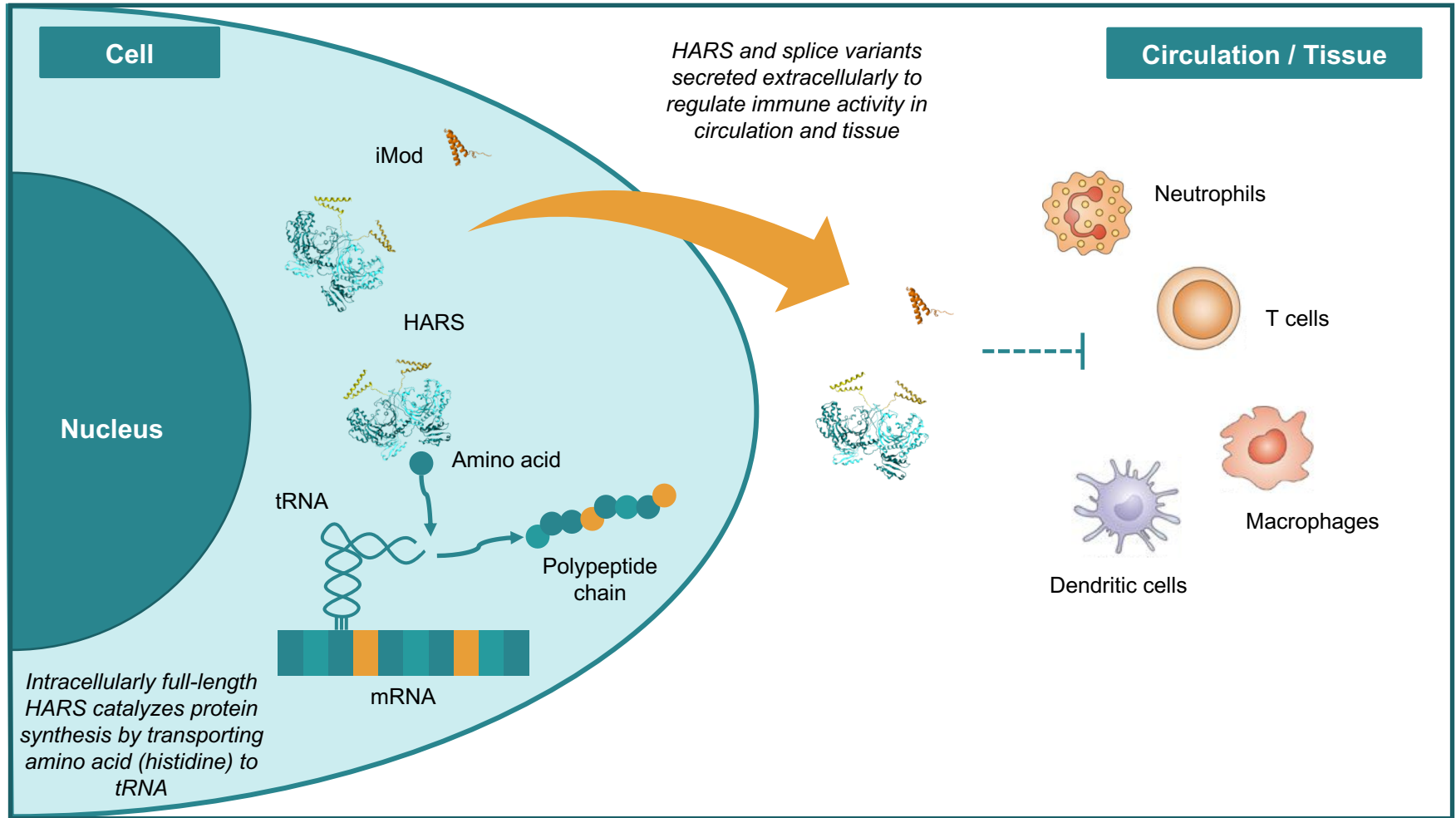
Clinical Milestones:

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

Development Pipeline

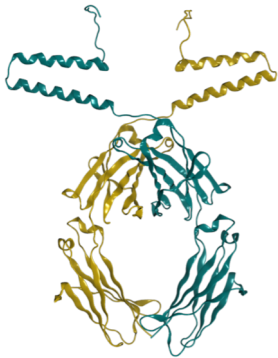


Novel tRNA Synthetase Domains Secreted Extracellularly with Non-Catalytic Functions



Extracellular tRNA Synthetase Biology Associated with Disease in Multiple Tissues

aTyr's current R&D focus



Drug: ATYR1923

Function: Immuno-modulatory

Disease: Interstitial Lung Disease

tRNA Synthetase Gene Families

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

aTyr patents cover >300 protein compositions

Pipeline opportunities

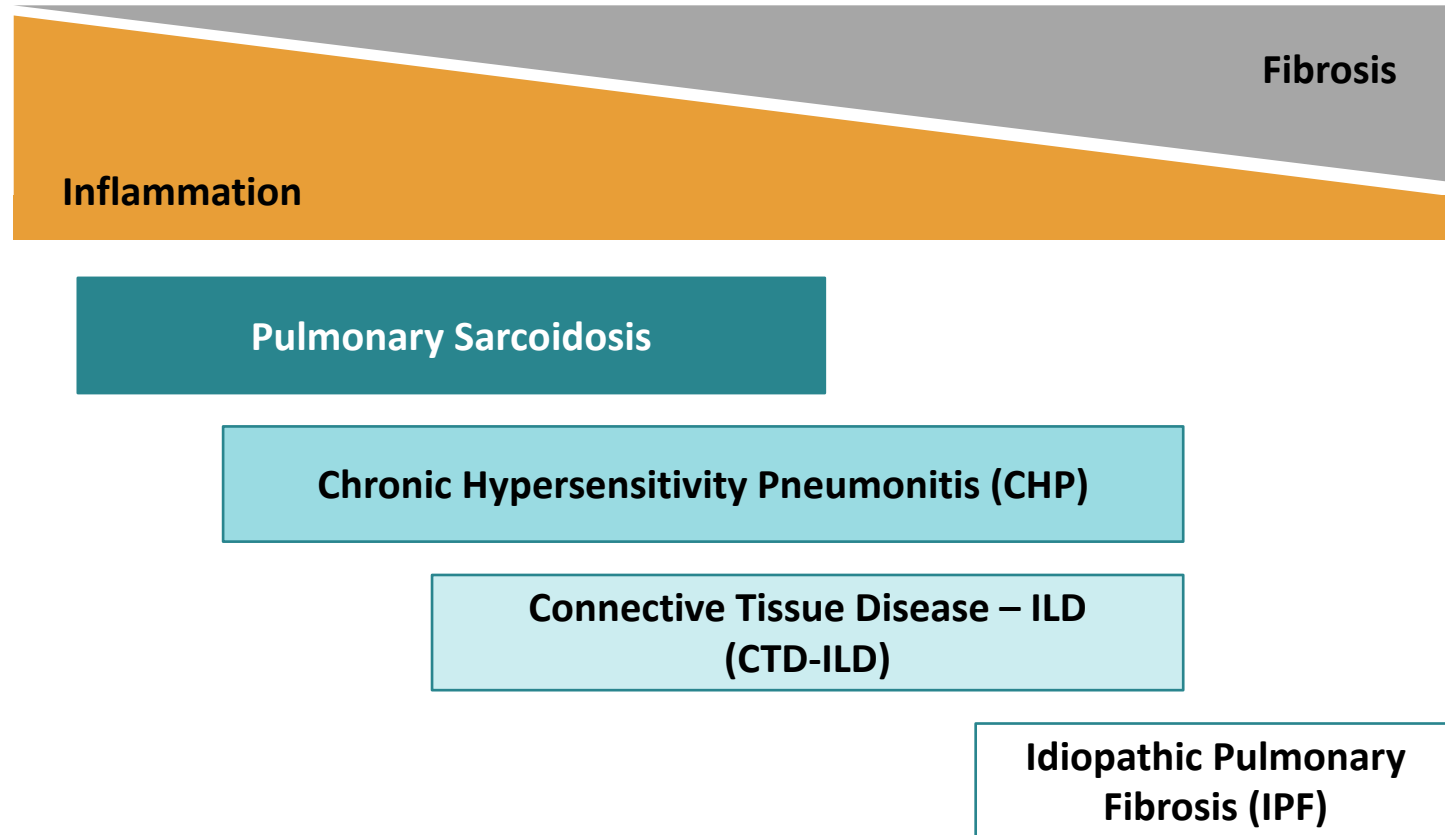
Known disease connections:

- Cancer
- Autoimmune disease
- Liver disorders
- Inflammatory disorders
- Neurological disorders
- Mitochondrial disorders

CSL Behring Collaboration:

- Potential new drug candidates from up to 4 tRNA synthetase families

Interstitial Lung Diseases Share Persistent Immune Engagement



High Unmet Need in Interstitial Lung Disease

Pulmonary Sarcoidosis

- Systemic inflammatory disorder characterized by non-caseating granulomas (CD4+ T cell driven)
- US prevalence: ~200k
- ~30% of patients have chronic progressive disease, unresponsive to steroid treatment
- Current SOC: steroids - cytotoxic agents - TNF inhibitors (as disease progresses)

Chronic Hypersensitivity Pneumonitis (CHP)

- Exaggerated immune response to environmental antigen
- US prevalence: ~60k
- 5-year mortality: ~20%
- No effective therapeutic options

Connective Tissue Disease-ILD (CTD-ILD)

- Common manifestation in CTD: Clinically relevant ILD in 10% of Rheumatoid Arthritis and >50% of Scleroderma patients
- US prevalence: ~150k
- 5-year mortality: ~20%
- Current SOC: Mycophenolate mofetil or cyclophosphamide for Ssc-ILD; no SOC for RA-ILD

Idiopathic Pulmonary Fibrosis (IPF)

- Irreversible, progressive fibrotic disease of unknown cause
- US prevalence: ~135k
- 5-year mortality: 60-80%
- Current SOC: Nintedanib or pirfenidone (>\$2b combined 2017 sales)

Pre-Clinical Translational Estate Supports Clinical Development in ILD

Bleomycin-Induced Lung Injury (Mouse)

- ATYR1923 vs. pirfenidone⁽¹⁾
- ATYR1923 reduced fibrosis and inflammation
- Presented at ATS, May 2017

Bleomycin-Induced Lung Injury (Rat)

- ATYR1923 vs. nintedanib⁽²⁾
- 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⁽²⁾
- ATYR1923 reduced lung and skin fibrosis
- Presented at Scleroderma Foundation Patient Conference, July 2018

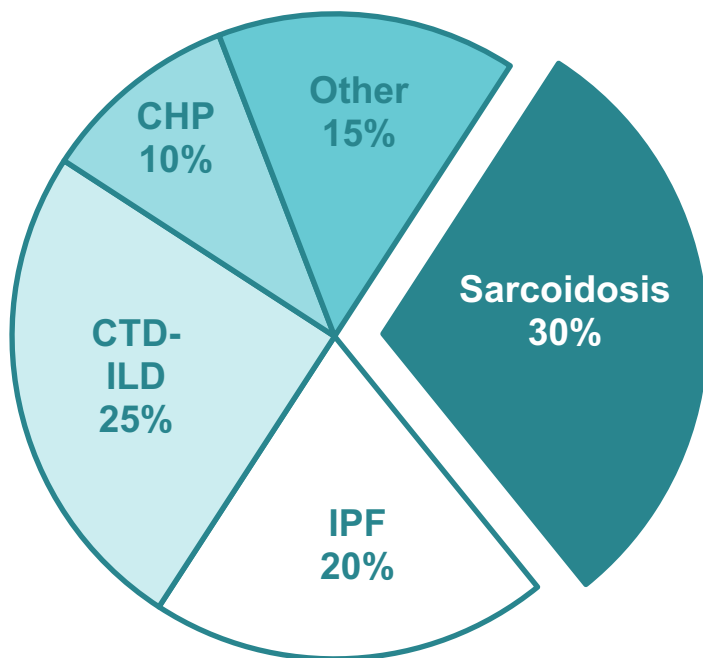


ATYR1923

For the Treatment of
Pulmonary Sarcoidosis

Sarcoidosis: The Most Common Form of Interstitial Lung Disease

Interstitial Lung Diseases



\$2-3b⁽¹⁾ Global Opportunity



50% require systemic therapy



30% with chronic progressive disease despite currently available treatment

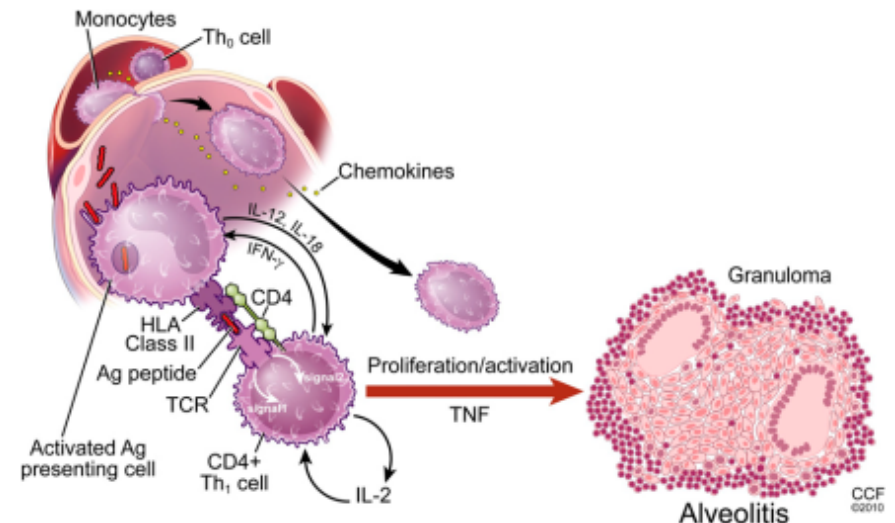


First-in-Patient Population: Pulmonary Sarcoidosis

- 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⁾:

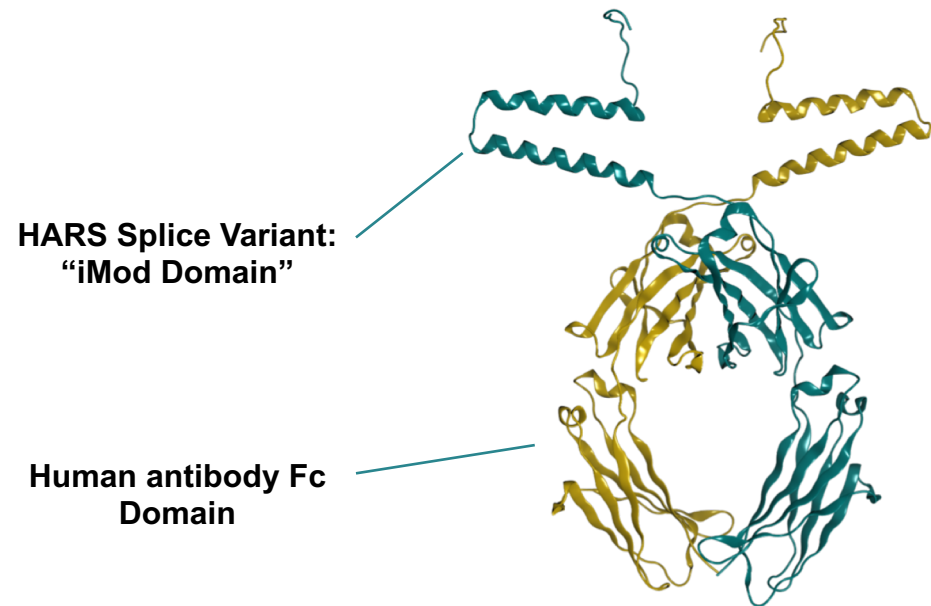
- Better understanding of pathogenesis
- Prognostic stratification and targeted management
- Better therapies, with quicker onset of action and less toxicity



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

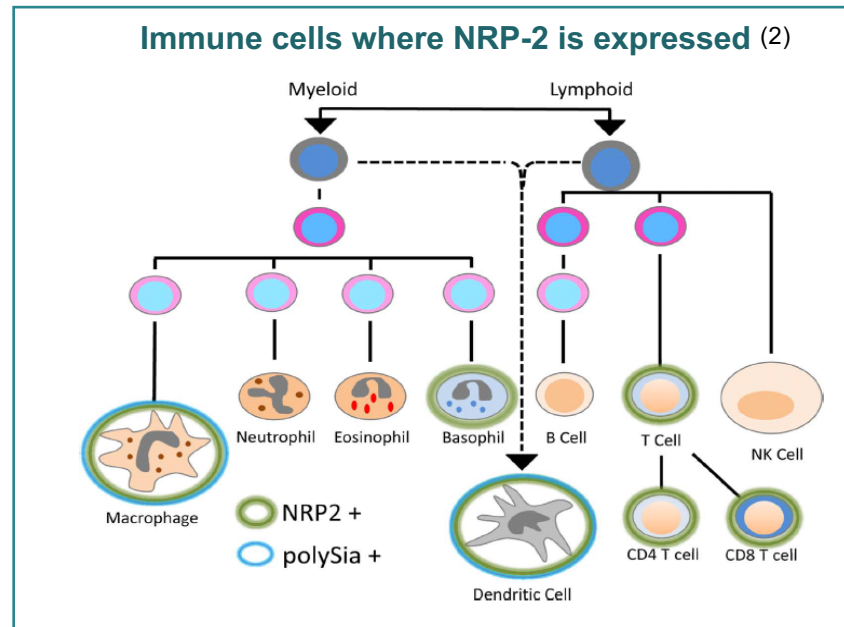
ATYR1923: Novel Engineered Protein Therapeutic

- 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

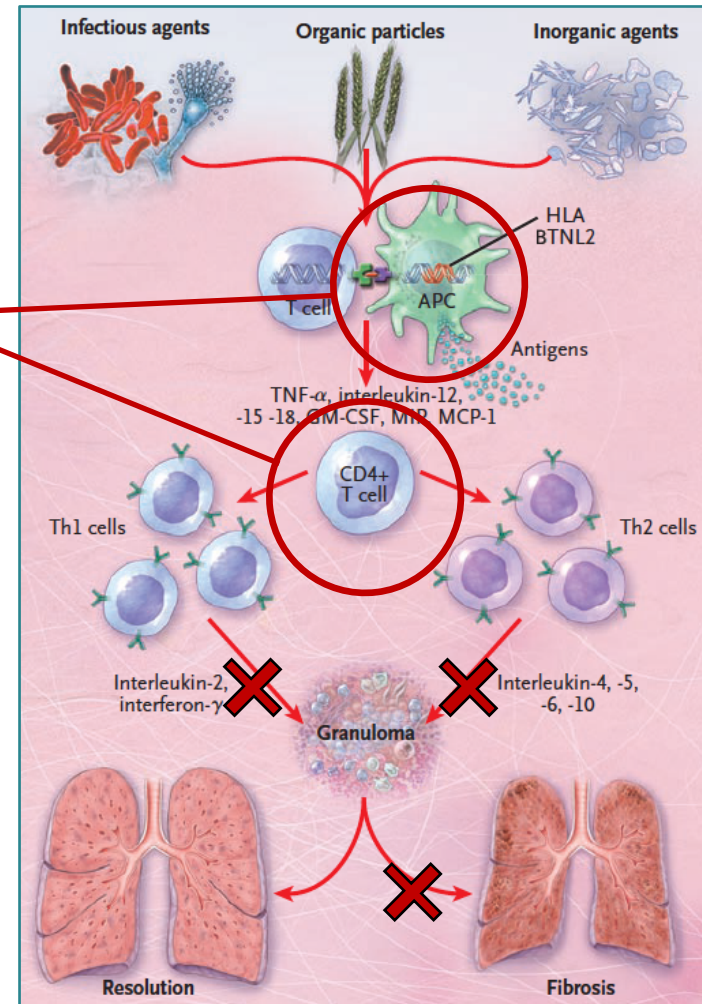
- Pleiotropic receptor that can bind to a number of different ligands
- Well-established role in the development of the neural and lymphatic systems
- Emerging role in the immune system; present on a number of immune cell types
- Expressed on alveolar macrophages; may play role in regulating lung inflammation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



ATYR1923 Intervention in Pulmonary Sarcoidosis

ATYR1923 Therapeutic Hypothesis⁽¹⁾:

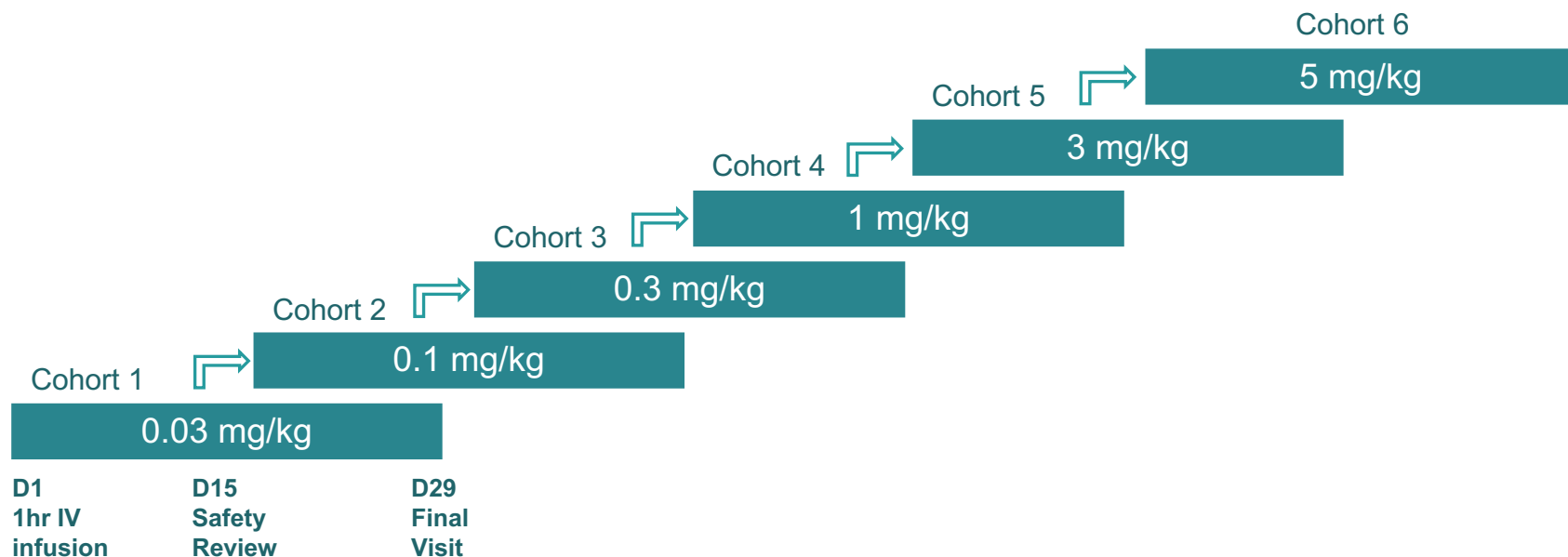
Downregulates inflammatory insult and prevents progression to fibrosis



PK Profile Supports Potential Once-Monthly Dosing

Phase 1 Healthy Volunteer Study Completed

- Positive 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



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 ^{18}F -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
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- Sites**
- Up to 15 leading pulmonary sarcoidosis centers in US
 - Collaboration with the Foundation for Sarcoidosis Research
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ATYR1923 Phase 1b/2a Study Endpoints

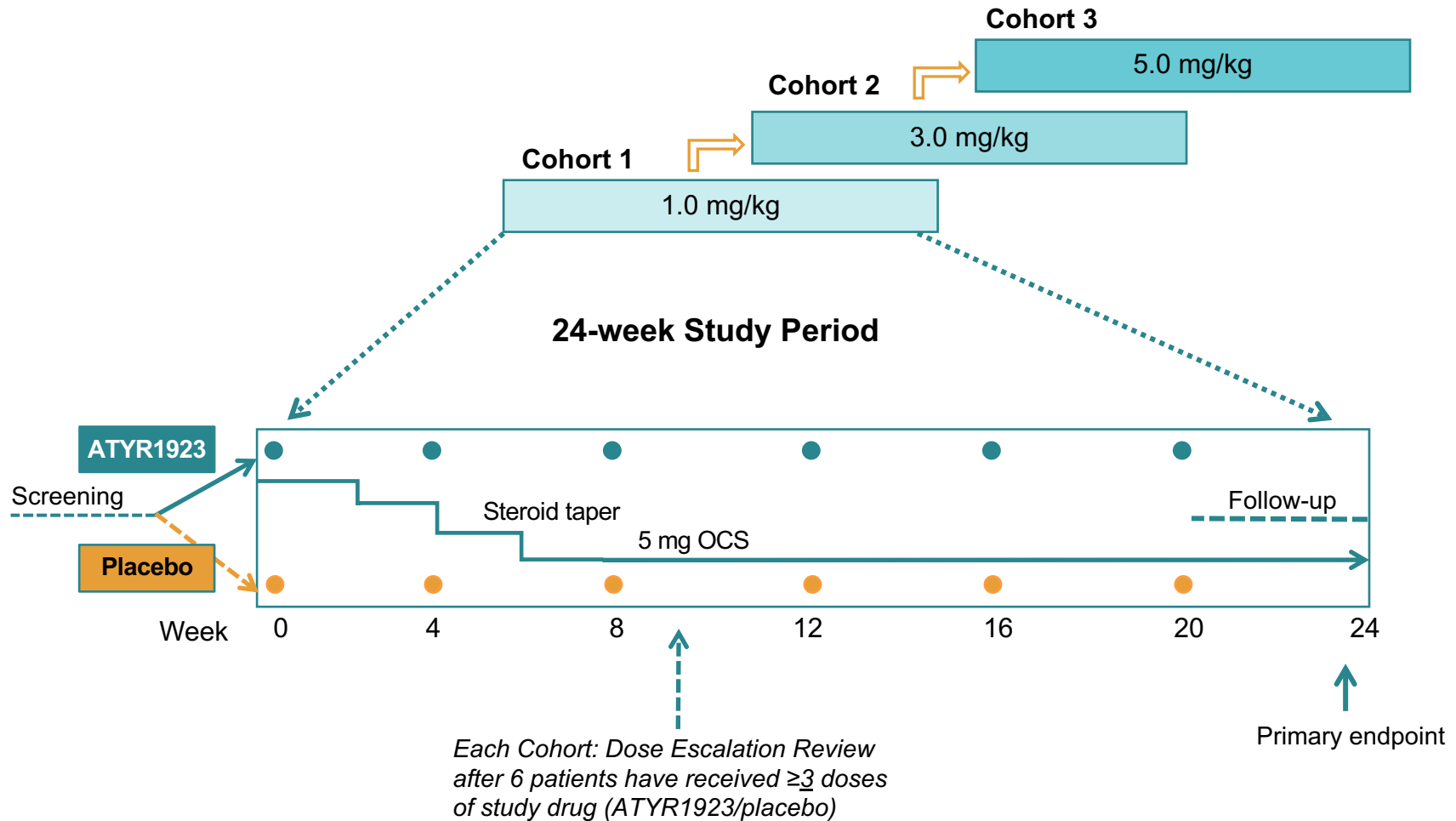
Primary

- 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	<ul style="list-style-type: none">• Up to 15 leading Pulmonary Sarcoidosis centers in US• Site initiation activities ongoing• Recruiting activities initiated
Timelines	<ul style="list-style-type: none">• Interim data: 4Q 2019• Study completion: mid-2020⁽¹⁾
Possible Future Development	<ul style="list-style-type: none">• Registrational trial in Pulmonary Sarcoidosis• Initiate P2 studies in other types of interstitial lung disease (e.g. CTD-ILD; CHP)

CSL Behring Collaboration

Goal

Identify new IND candidates from up to four tRNA synthetases from aTyr's proprietary pipeline of novel proteins (non-HARS derived)

Terms

- CSL Behring to fund all R&D costs
 - aTyr eligible for up to \$17m in option fees if CSL Behring advances all four programs (\$4.25m per synthetase program)
 - aTyr grants CSL Behring an option to negotiate licenses for worldwide rights to each IND candidate that emerges from the collaboration
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About CSL

- CSL Behring is a global biotherapeutics leader specializing in immunology, hematology and other rare and serious medical conditions
 - CSL Behring employs >22,000 people globally, and delivers its therapies to more than 60 countries
-

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 ATYR1923 into other ILD indications
- Potential new pipeline opportunities through academic (UNMC) and industry (CSL Behring) collaborations



Thank You