



A New Path to Medicine

H.C. Wainwright 21st Annual Global Investment Conference

Sanjay S. Shukla, M.D., M.S., President & CEO

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Forward-Looking Statements

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aTyr Pharma Company Overview

Accelerating Value Creation from New 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 \$42.4m as of 6/30/2019

April 2019: \$5m raise with Federated and Dr. Paul Schimmel, board member, at market, no discount or warrants

Clinical Milestones:

Initiated P1b/2a Trial – Q4 2018

- ☐ Interim Safety – Q4 2019
- ☐ Final Results – mid-2020⁽²⁾

(1) aTyr estimates for inflammatory ILD: Pulmonary Sarcoidosis, CHP, CTD-ILD; excludes IPF

(2) Dependent on patient enrollment

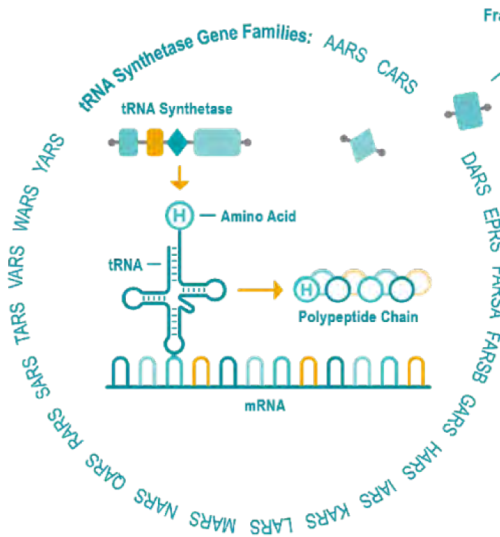
Development Pipeline

PROGRAM	DISEASES	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 1B/2	PHASE 2/3
ATYR1923	Pulmonary Sarcoidosis					
	Chronic Hypersensitivity Pneumonitis (CHP)					
	Connective Tissue Disease ILD (CTD-ILD)					
tRNA Synthetase Candidates	Undisclosed		CSL Behring			
NRP2 Candidates	Undisclosed					

Extracellular tRNA Synthetase Biology

INTRACELLULAR

Catalyze Protein Synthesis



EXTRACELLULAR

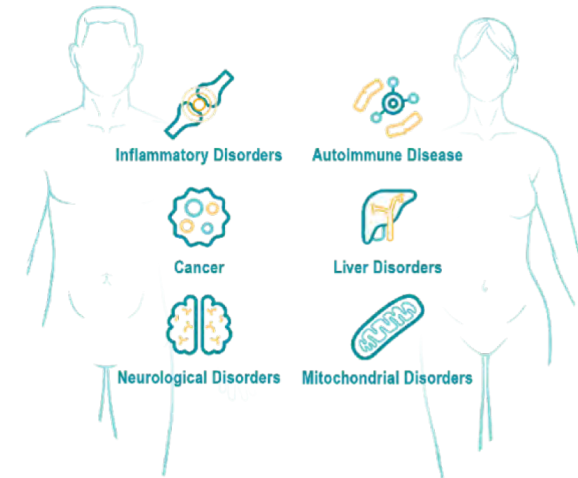
Secreted in Circulation and Tissue to Regulate Diverse Pathways

Fragments and Splice Variants



PHYSIOLOGICAL

Pathway Disruption Associated with Disease



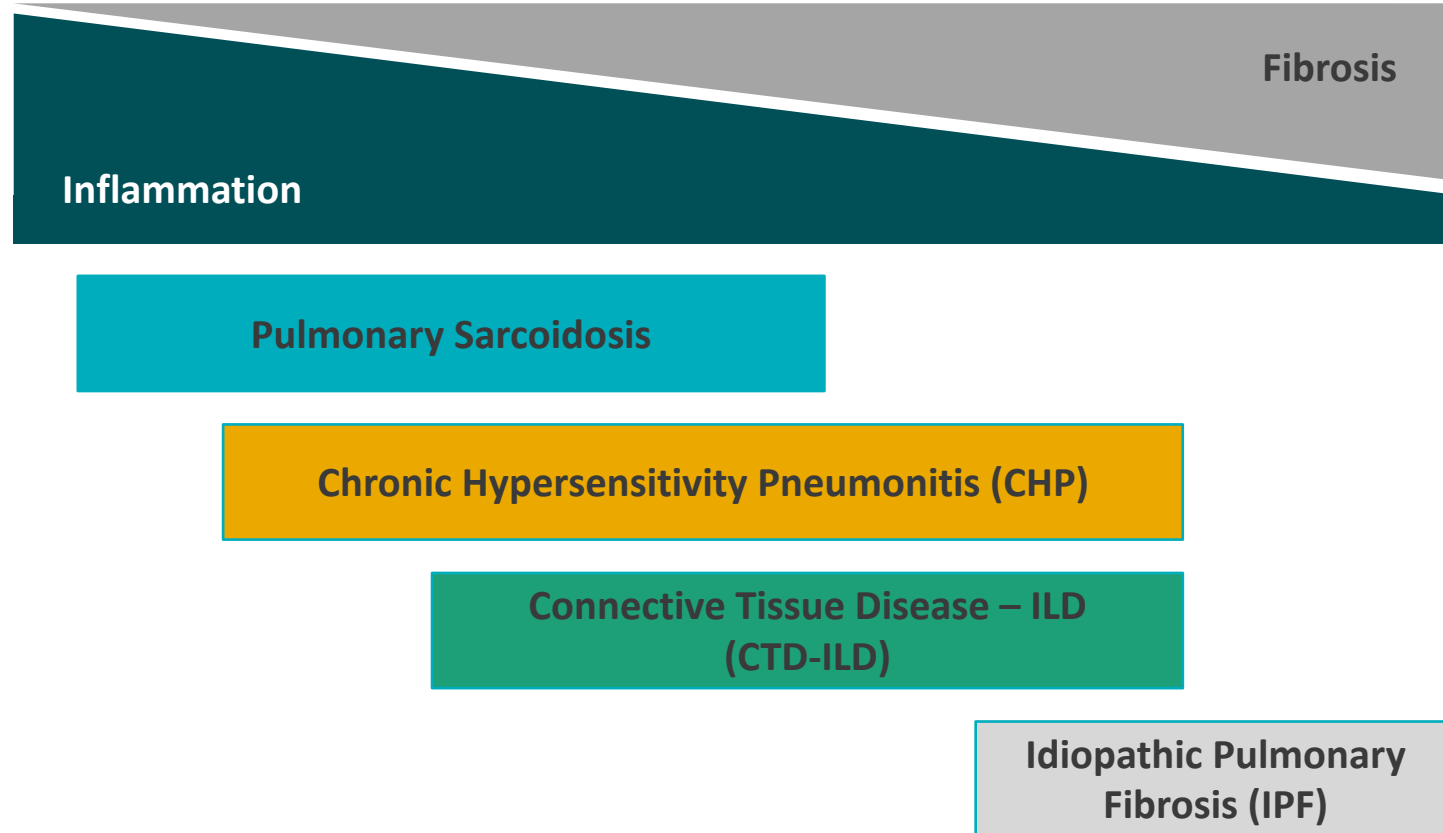
CSL Behring Collaboration

Goal	<ul style="list-style-type: none">• Identify new IND candidates from up to four tRNA synthetases from aTyr's proprietary pipeline of novel proteins (non-HARS derived)
Terms	<ul style="list-style-type: none">• 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
About CSL	<ul style="list-style-type: none">• 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
Status	<ul style="list-style-type: none">• aTyr received first phase of funding totaling \$630k, and of that recognized \$94k of collaboration revenue in Q2 2019



ATYR1923
For the Treatment of
Pulmonary Sarcoidosis

ILDs Share Persistent Immune Engagement



High Unmet Need Persists

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)

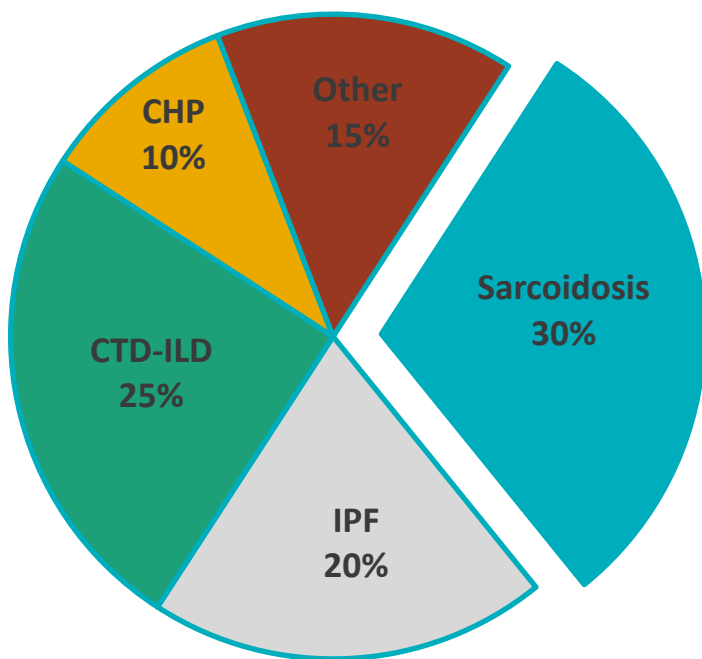
- Common manifestation in CTD: Clinically relevant ILD in 10% of Rheumatoid Arthritis and >50% of Scleroderma patients
- US prevalence: ~150k
- 5-year mortality: ~20%
- Current SOC: Mycophenolate mofetil or cyclophosphamide for Ssc-ILD; no SOC for RA-ILD
- Nintedanib approval September 2019

Idiopathic Pulmonary Fibrosis (IPF)

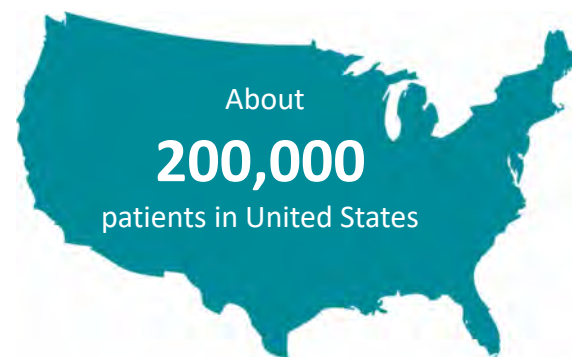
- Irreversible, progressive fibrotic disease of unknown cause
- US prevalence: ~135k
- 5-year mortality: 60-80%
- Current SOC: Nintedanib or pirfenidone (>\$2.2b combined 2018 net revenue)

Sarcoidosis: A Major Form of ILD

ILD Patient Distribution



\$2-3b Global Opportunity⁽¹⁾



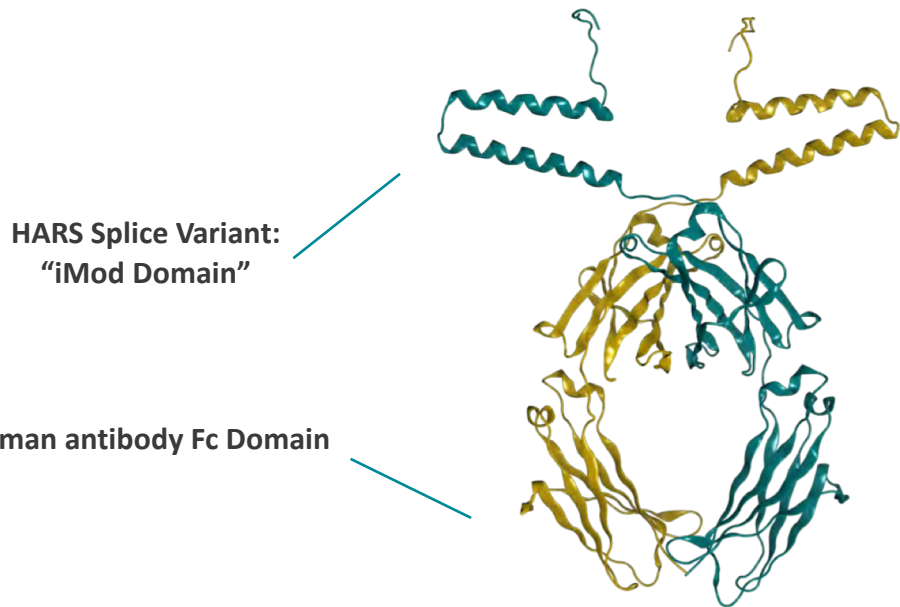
50% require systemic therapy



30% with chronic progressive disease despite currently available treatment

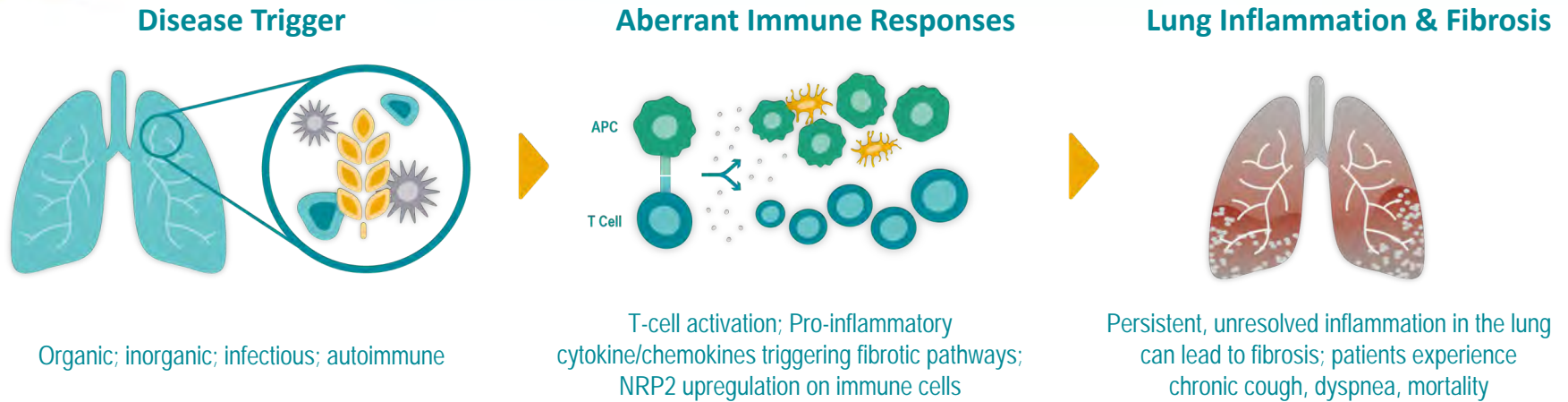


ATYR1923: Novel Engineered Protein Therapeutic

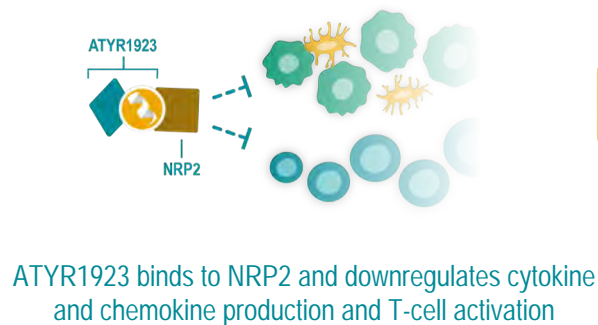


- iMod Domain of HARS enriched in the human lung
- Inhibits human T cell activation/cytokine release
- Binds selectively to Neuropilin-2 (NRP2)
- Regulates a number of immune cell-types, including: T cells, Neutrophils, Macrophages, Dendritic cells
- iMod Domain fused to Fc Domain to extend half-life
- Once-monthly IV dosing regimen

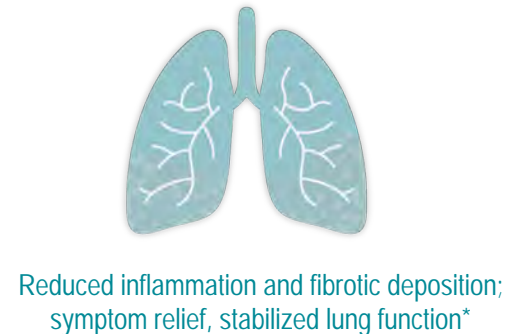
ATYR1923 Mechanism of Action in ILD



ATYR1923 Dampens Immune Responses



Stabilized Lung



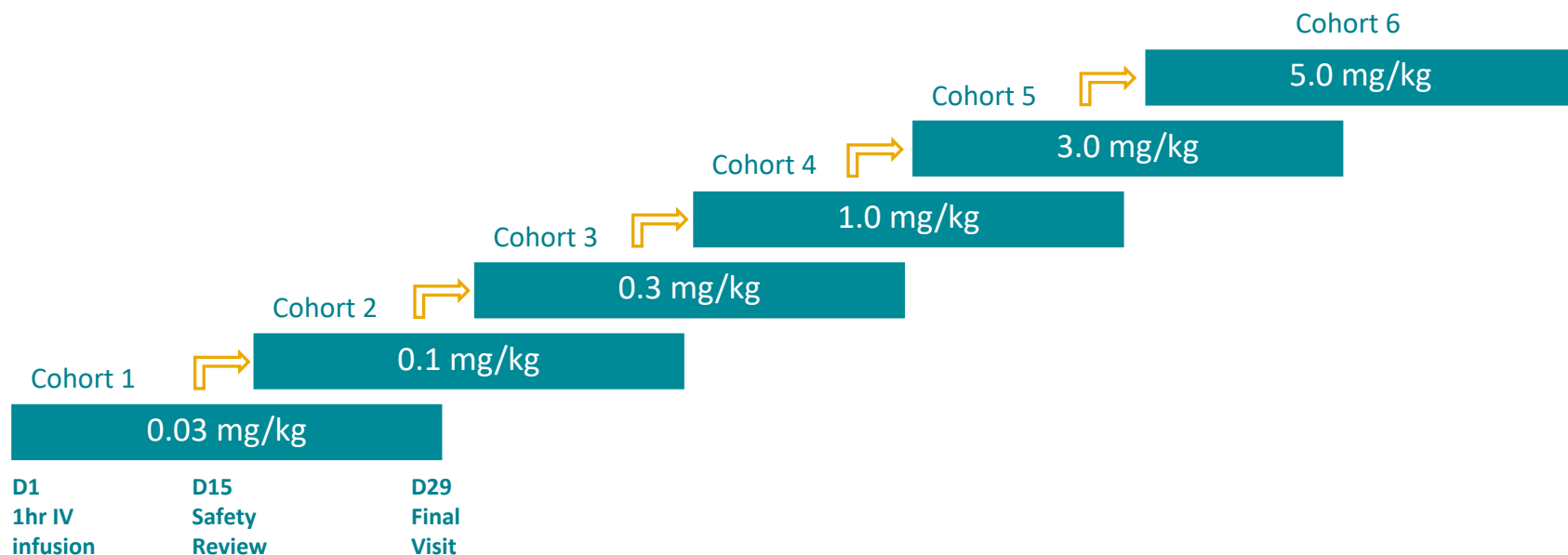
Pre-Clinical Translational Data Supports ILD Development

Bleomycin-Induced Lung Injury (IPF) – Mouse	<ul style="list-style-type: none">• ATYR1923 reduced fibrosis and inflammation• Comparator: pirfenidone• Presented at ATS, May 2017
Bleomycin-Induced Lung Injury (IPF) – Rat	<ul style="list-style-type: none">• ATYR1923 returned lung function to normal and reduced fibrosis and inflammation• Comparator: nintedanib• Presented at ATS, May 2018
Sclerodermatous chronic-graft vs host disease (SSc-ILD) – Mouse	<ul style="list-style-type: none">• ATYR1923 reduced lung and skin fibrosis• Comparator: nintedanib• Presented at Scleroderma Foundation Patient Conference, July 2018
SSc-cGVHD (SSc-ILD); <i>P. acnes</i> (Sarcoidosis); <i>S. rectivirgula</i> (CHP); SKG (Ra-ILD) – Mouse	<ul style="list-style-type: none">• ATYR1923 demonstrated stage-dependent anti-inflammatory and anti-fibrotic effect in various experimental models of ILD• Comparator: various• Presented at ATS, May 2019

PK Profile Supports Potential Once-Monthly Dosing

Phase 1 Healthy Volunteer Study Completed in Australia

- 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	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Randomized, double-blind, placebo-controlled, multiple ascending dose
Population	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 3 sequential cohorts, 12 patients each• 2:1 randomization• ATYR1923 doses: 1.0, 3.0, and 5.0 mg/kg
Duration	<ul style="list-style-type: none">• 24-week study period• Steroid taper phase down to 5 mg by week 8• 16-week maintenance phase
Sites	<ul style="list-style-type: none">• Up to ~15 leading pulmonary sarcoidosis centers• Collaboration with the Foundation for Sarcoidosis Research

ATYR1923 Phase 1b/2a Study Endpoints

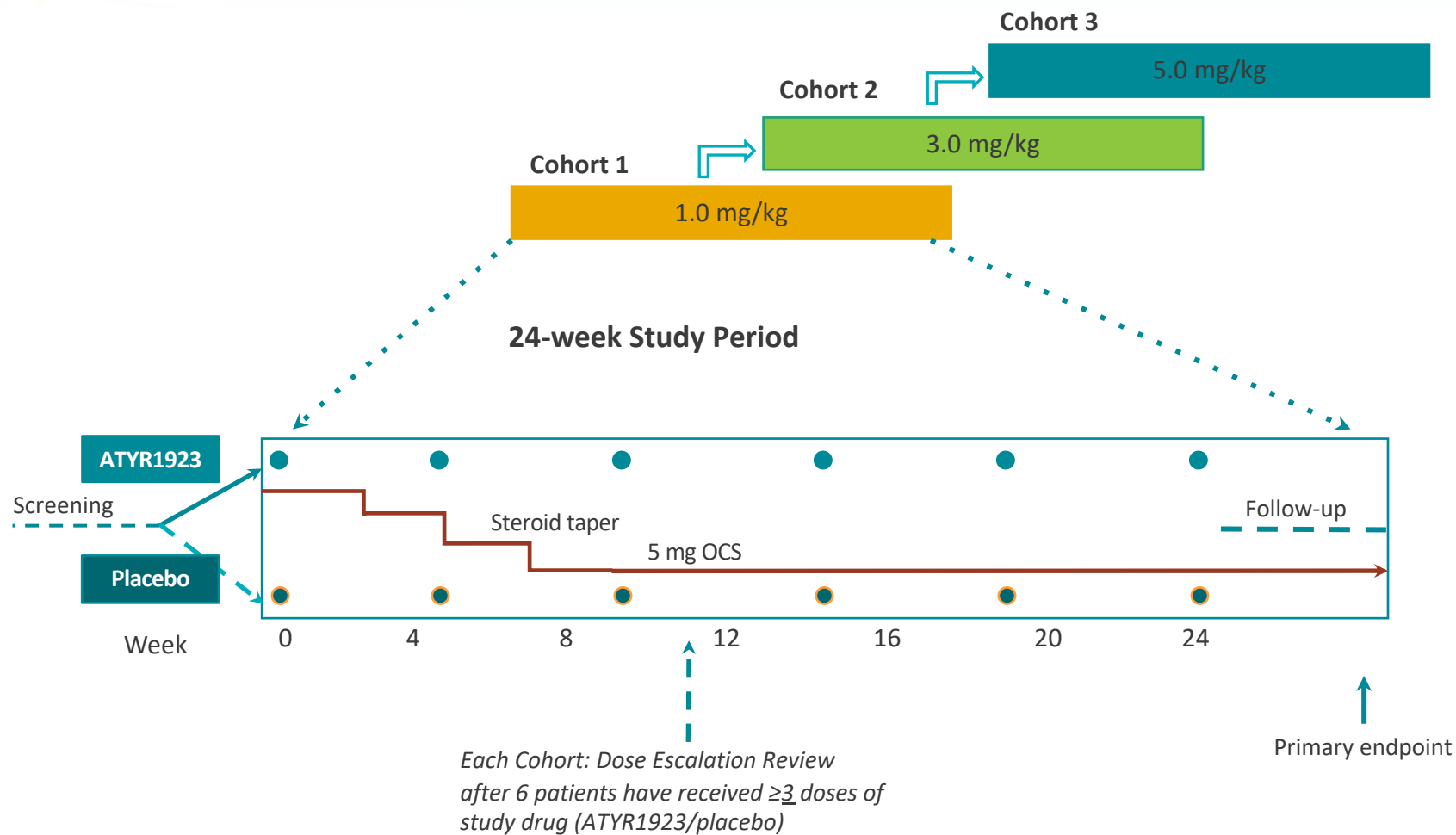
Primary

- 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

Phase 1b/2a Study Schema



ATYR1923 Phase 1b/2a Study in Pulmonary Sarcoidosis

Status

- Up to 15 leading Pulmonary Sarcoidosis centers
- New site activation ongoing
- Patient enrollment ongoing

Timelines

- Interim safety data: Q4 2019
- Study completion: mid-2020⁽¹⁾

Possible Future Development

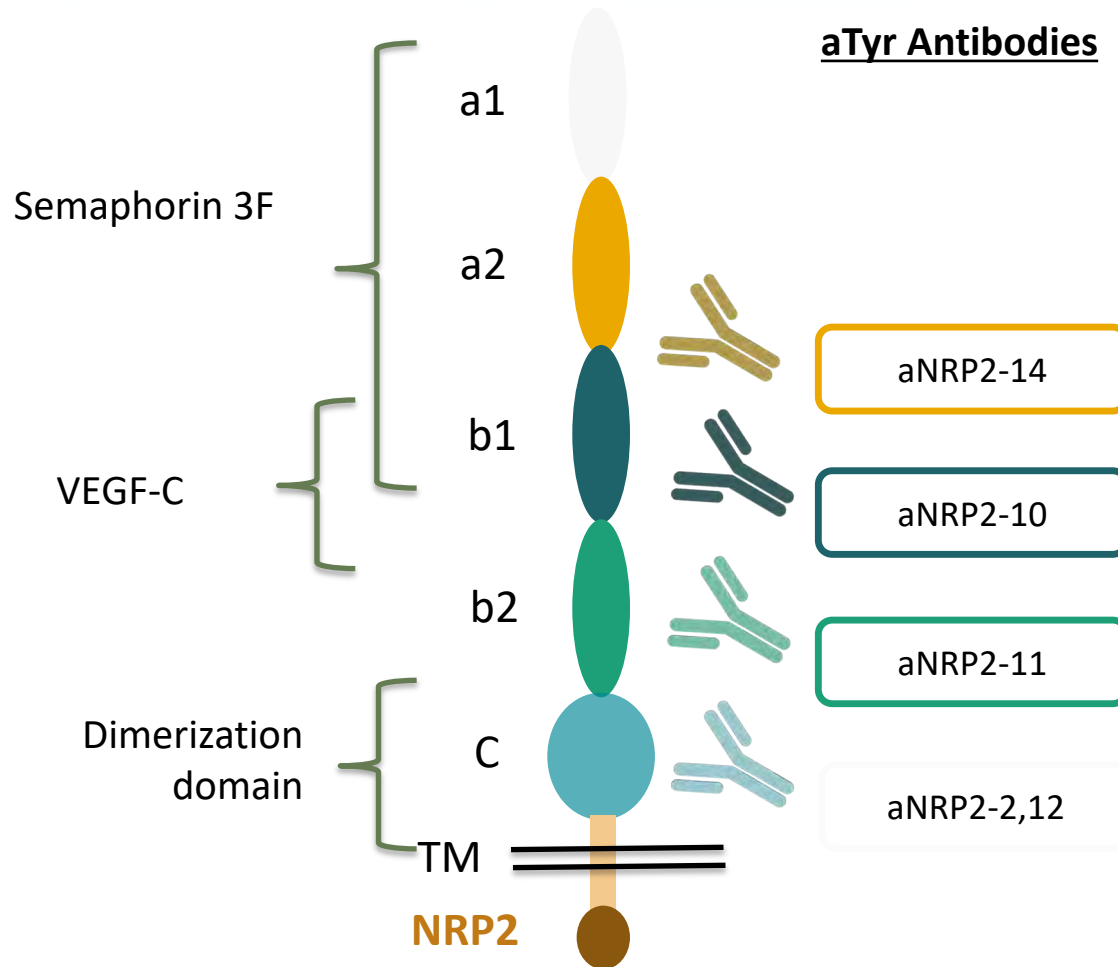
- Registrational trial in Pulmonary Sarcoidosis
- Initiate P2 studies in other types of interstitial lung disease (e.g. CTD-ILD; CHP)

(1) Dependent on patient enrollment

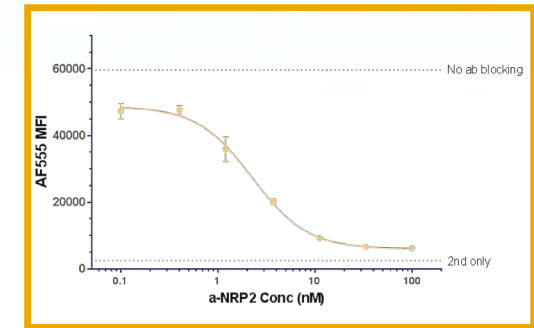


NRP2 Biology

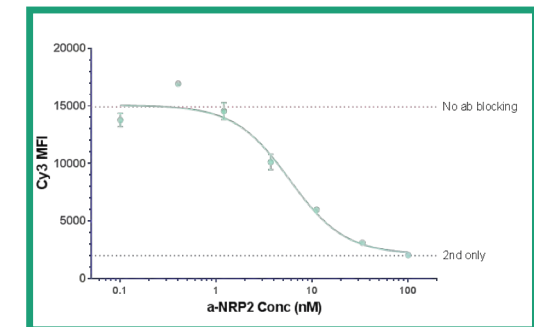
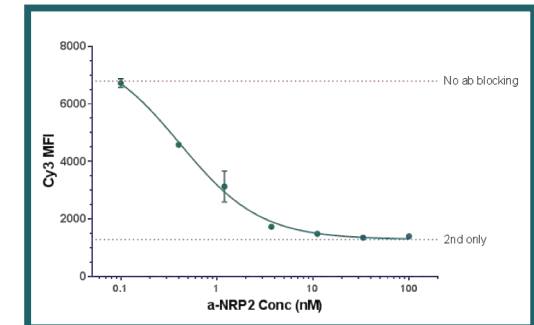
aTyr NRP2 Blocking Antibodies



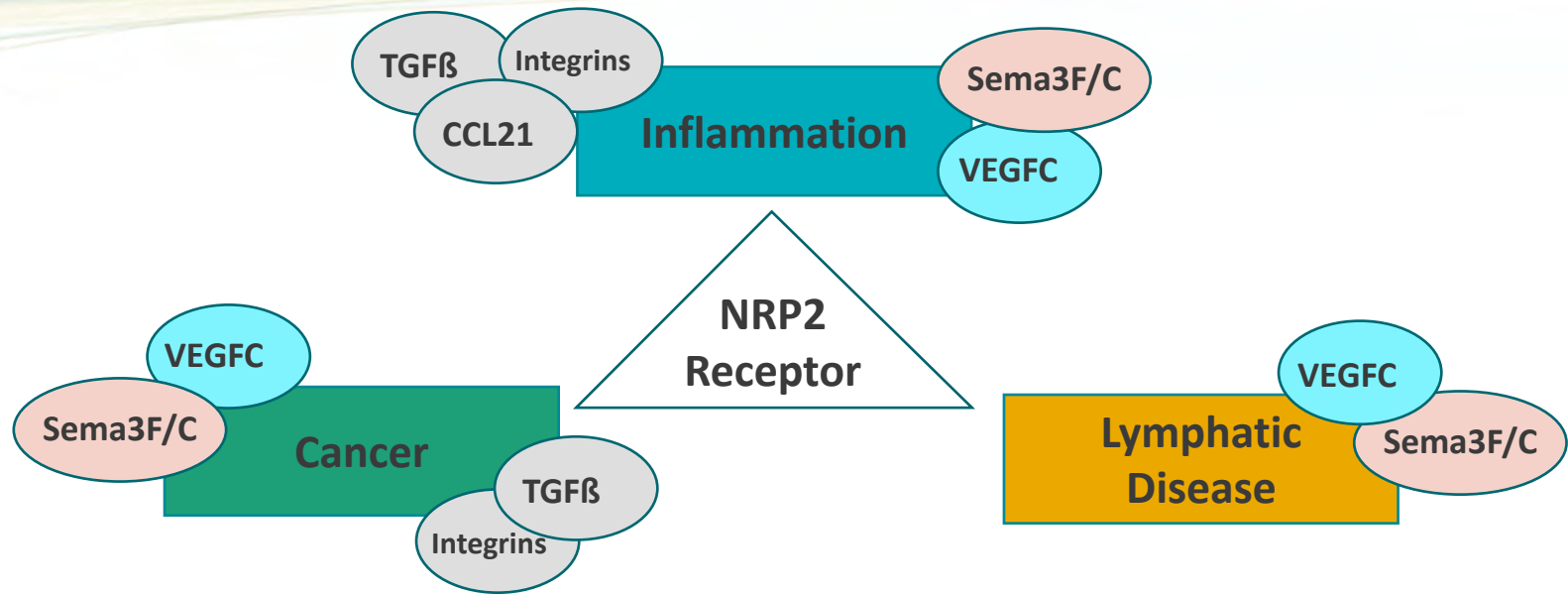
Sema3F Blocking



VEGF-C Blocking



NRP2 Receptor Biology Associated with Diverse Pathways



- Implicated in cancer, inflammation and lymphatic disease
- Co-receptors for semaphorins and VEGF family molecules
- Overexpressed in various tumors, tumor expression linked to poor prognosis
- Critical for cancer cell migration, metastasis, EMT, lymphangiogenesis

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 NRP2 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 and industry collaborations



Thank You