



# A New Path to Medicine

Stifel 2019 Healthcare Conference

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# aTyr Pharma

## Company Overview

# aTyr: A New Path to Medicine

- Focus: translating novel biological pathways into first-in-class therapeutics
- Lead drug candidate ATYR1923 enrolling Phase 1b/2a trial in pulmonary sarcoidosis
  - Potential for rapid expansion into other interstitial lung diseases with a total estimated \$2-3b global opportunity<sup>(1)</sup>
  - Interim safety data December 2019
  - Final results mid-2020<sup>(2)</sup>
- Pipeline of Neuropilin-2 (NRP2) antibodies and tRNA synthetase candidates
- Broad IP estate covering pipeline of tRNA synthetase protein compositions and certain associated pathways
- Cash, cash equivalents and investments at \$38.1m as of 9/30/19

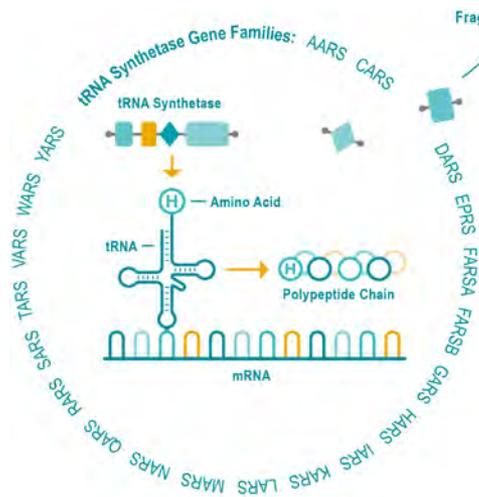
# aTyr Development Pipeline

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

# Novel Functions of tRNA Synthetases

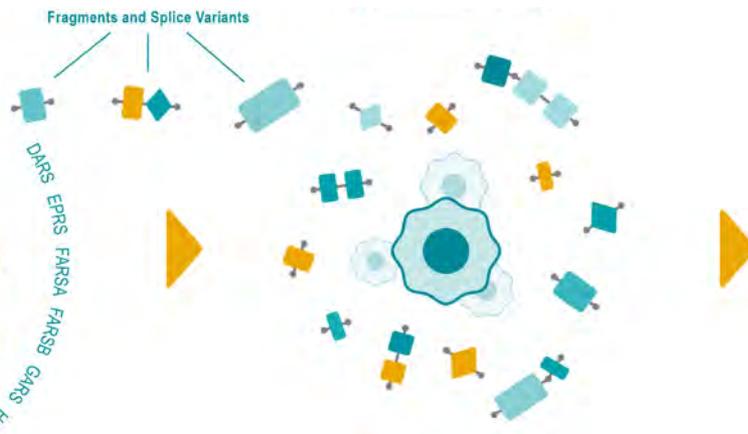
## INTRACELLULAR

Catalyze Protein Synthesis



## EXTRACELLULAR\*

Secreted in Circulation and Tissue to Regulate Diverse Pathways



## PHYSIOLOGICAL

Pathway Disruption Associated with Disease



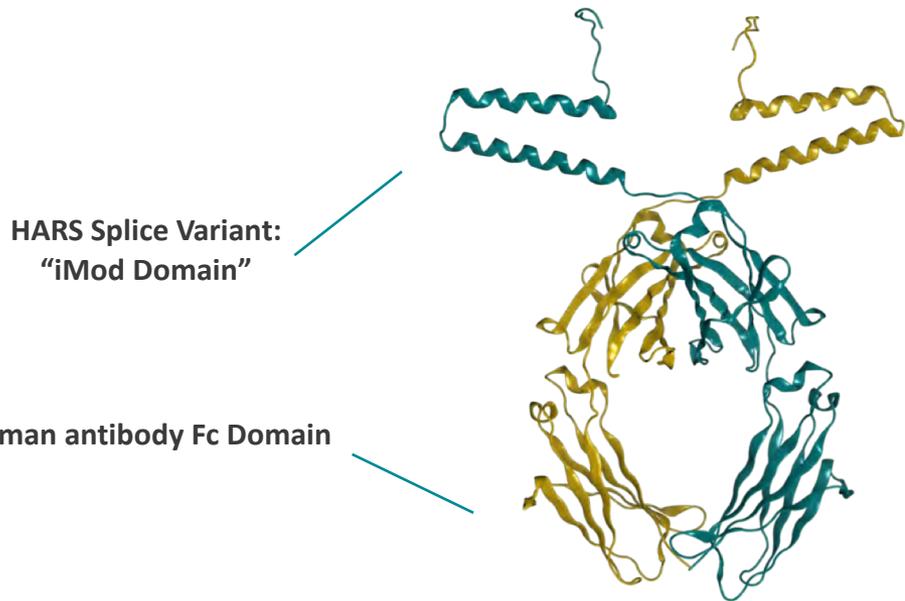
# CSL Behring Collaboration

<b>Goal</b>	<ul style="list-style-type: none"><li>• Identify new IND candidates from up to four tRNA synthetases from aTyr's proprietary pipeline of novel proteins (non-HARS derived)</li></ul>
<b>Terms</b>	<ul style="list-style-type: none"><li>• CSL Behring to fund all R&amp;D costs</li><li>• aTyr eligible for up to \$17m in option fees if CSL Behring advances all four programs (\$4.25m per synthetase program)</li><li>• aTyr grants CSL Behring an option to negotiate licenses for worldwide rights to each IND candidate that emerges from the collaboration</li></ul>
<b>About CSL</b>	<ul style="list-style-type: none"><li>• CSL Behring is a global biotherapeutics leader specializing in immunology, hematology and other rare and serious medical conditions</li><li>• CSL Behring employs &gt;22,000 people globally, and delivers its therapies to more than 60 countries</li></ul>
<b>Status</b>	<ul style="list-style-type: none"><li>• aTyr received first phase of funding totaling \$630k, and of that recognized \$278k of collaboration revenue through Q3 2019</li></ul>



**ATYR1923**  
For the Treatment of  
Pulmonary Sarcoidosis

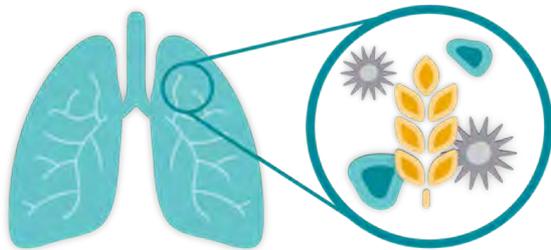
# ATYR1923: Novel Engineered Protein Therapeutic



- 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
- NRP2 expression in granulomas identified in sarcoidosis patients
- iMod Domain fused to Fc Domain to extend half-life
- Once-monthly IV dosing regimen

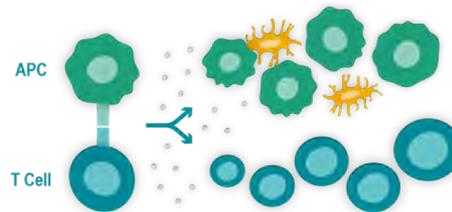
# ATYR1923 Mechanism of Action in ILD

## Disease Trigger



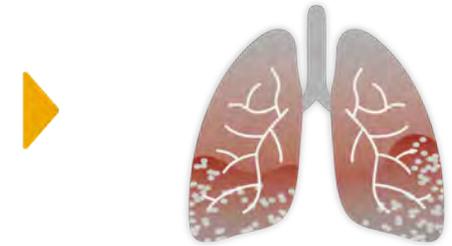
Organic; inorganic; infectious; autoimmune

## Aberrant Immune Response



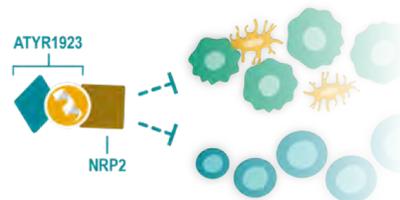
T-cell activation; pro-inflammatory cytokines/chemokines triggering fibrotic pathways; NRP2 upregulation on immune cells

## Lung Inflammation & Fibrosis



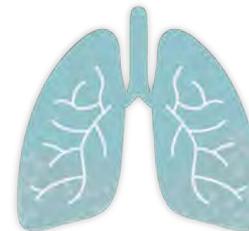
Persistent, unresolved inflammation in the lung can lead to fibrosis; patients experience chronic cough, dyspnea, mortality

## ATYR1923 Dampens Immune Responses



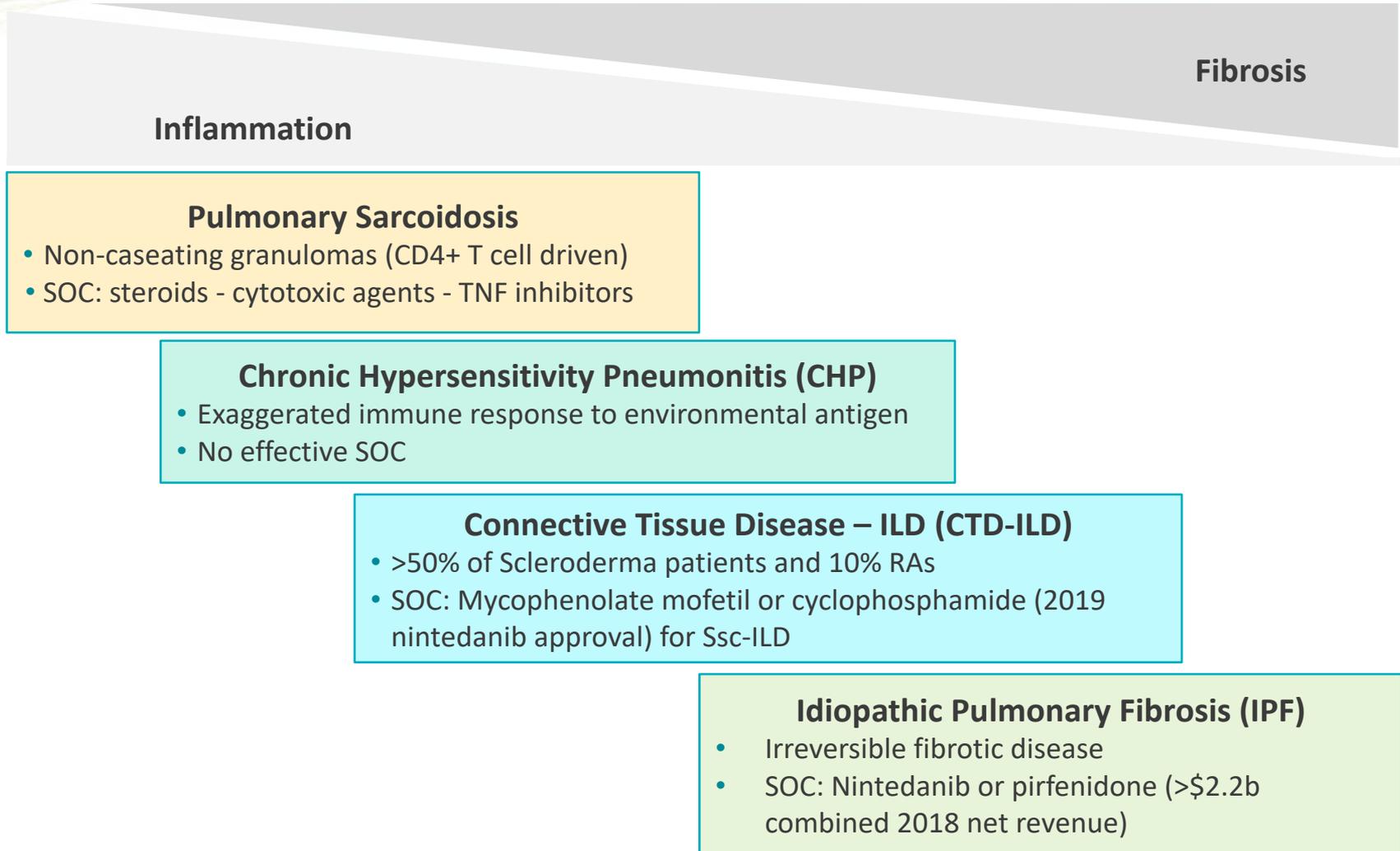
ATYR1923 binds to NRP2 and downregulates cytokine and chemokine production and T-cell activation

## Stabilized Lung



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

# ILDs Share Persistent Immune Engagement



# Pre-Clinical Translational Data Supports ILD Development

## **Bleomycin-Induced Lung Injury (IPF) – Mouse**

- ATYR1923 reduced fibrosis and inflammation
- Comparator: pirfenidone
- Presented at ATS, May 2017

## **Bleomycin-Induced Lung Injury (IPF) – Rat**

- ATYR1923 returned lung function to normal and reduced fibrosis and inflammation
- Comparator: nintedanib
- Presented at ATS, May 2018

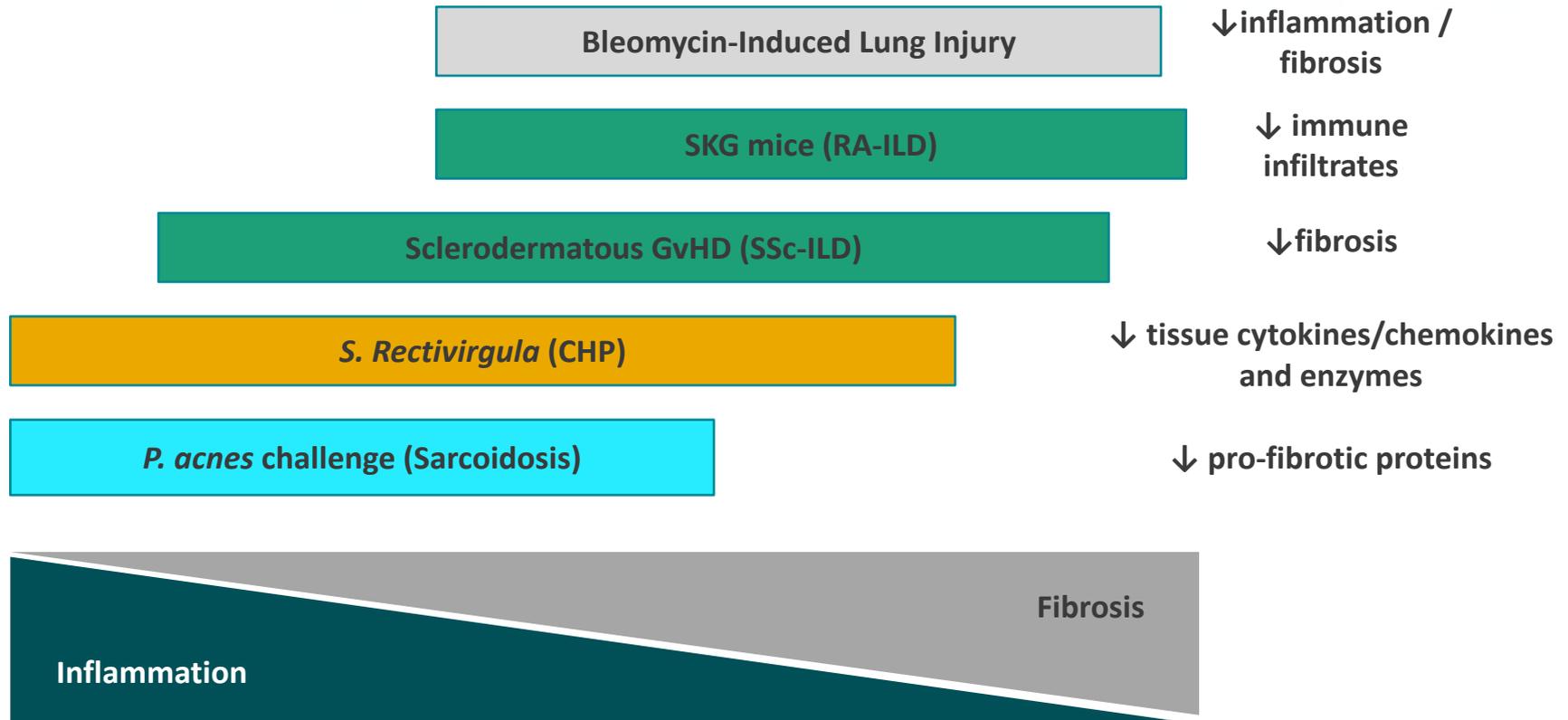
## **Sclerodermatous chronic-graft vs host disease (SSc-ILD) – Mouse**

- ATYR1923 reduced lung and skin fibrosis
- Comparator: nintedanib
- Presented at Scleroderma Foundation Patient Conference, July 2018

## **SSc-cGVHD (SSc-ILD); *P. acnes* (Sarcoidosis); *S. rectivirgula* (CHP); SKG (Ra-ILD) – Mouse**

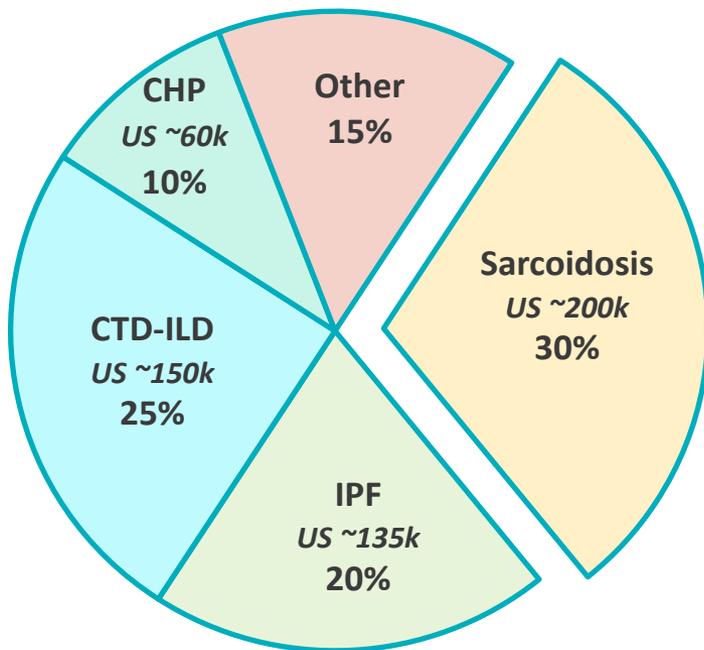
- ATYR1923 demonstrated stage-dependent anti-inflammatory and anti-fibrotic effect in various experimental models of ILD
- Comparator: various
- Presented at ATS, May 2019

# Demonstrated Effect in Multiple ILD Models



# Sarcoidosis: A Major Form of ILD

## ILD Patient Distribution



**\$2-3b Global Opportunity<sup>(1)</sup>**



50% require systemic therapy



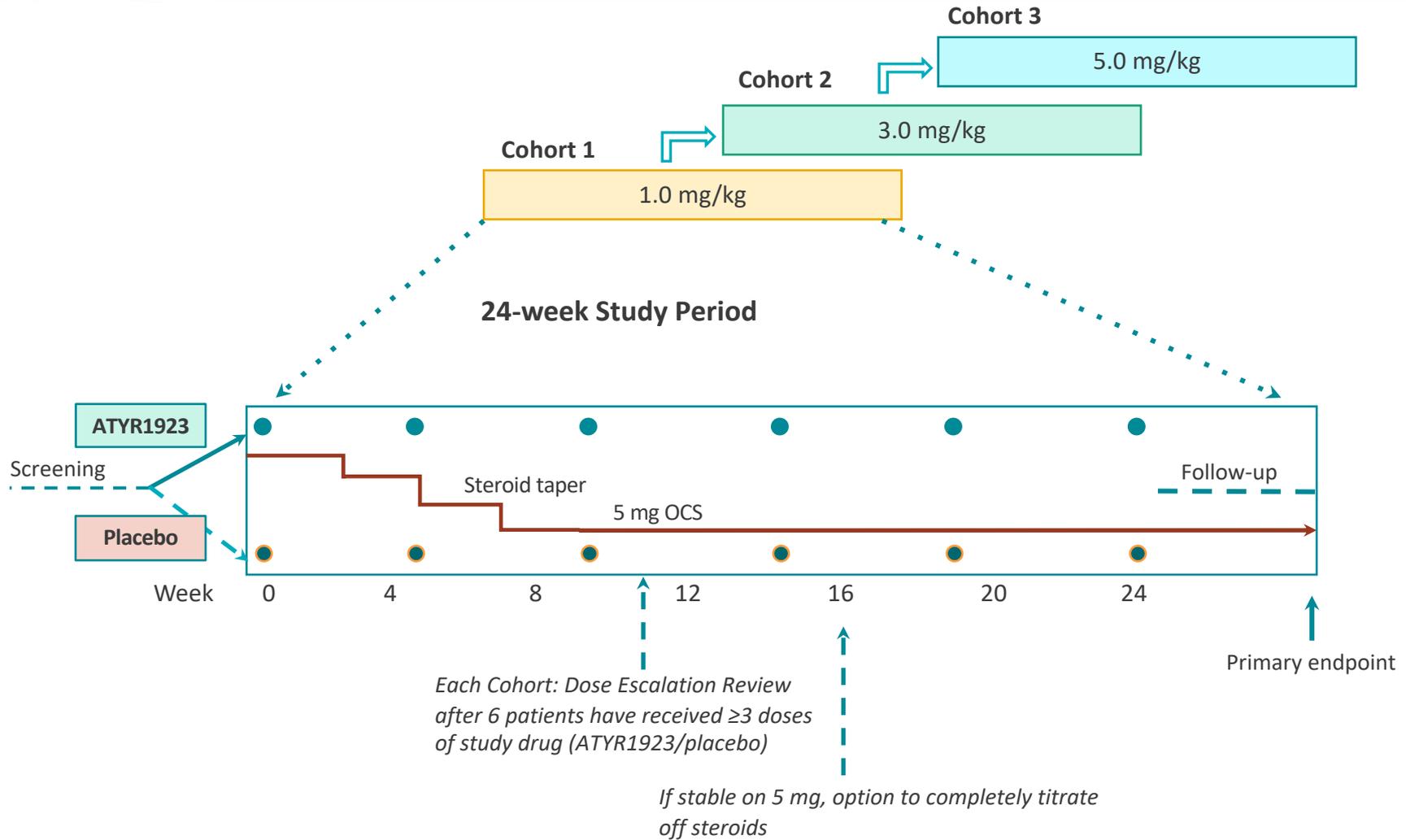
30% with chronic progressive disease despite currently available treatment



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

<b>Design</b>	<ul style="list-style-type: none"><li>• Randomized, double-blind, placebo-controlled, multiple ascending dose</li></ul>
<b>Population</b>	<ul style="list-style-type: none"><li>• Histologically confirmed pulmonary sarcoidosis</li><li>• Requiring <math>\geq 10</math> mg prednisone (steroid) treatment; capable of steroid taper</li><li>• Symptomatic/active disease at baseline by <math>^{18}\text{F}</math>-FDG-PET/CT, Pulmonary Function Tests</li></ul>
<b>Dosing</b>	<ul style="list-style-type: none"><li>• 3 sequential cohorts, 12 patients each, 2:1 randomization</li><li>• ATYR1923 doses: 1.0, 3.0, and 5.0 mg/kg</li></ul>
<b>Duration</b>	<ul style="list-style-type: none"><li>• 24-week study period</li><li>• Steroid taper phase down to 5.0 mg by week 8– by week 16, if stable, option to completely titrate off steroids</li></ul>
<b>Endpoints</b>	<ul style="list-style-type: none"><li>• Primary<ul style="list-style-type: none"><li>◦ Safety and tolerability of multiple ascending IV ATYR1923 doses</li></ul></li><li>• Secondary<ul style="list-style-type: none"><li>◦ Steroid-sparing effect</li><li>◦ Immunogenicity</li><li>◦ Pharmacokinetics (PK)</li><li>◦ Exploratory efficacy measures: FDG-PET/CT imaging; Lung function (FVC); Serum biomarkers; Health-related quality of life scales</li></ul></li></ul>

# Phase 1b/2a Study Schema



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

## Status

- Phase 1 in 36 healthy volunteers complete
- Patient enrollment ongoing in Phase 1b/2a in ~15 leading pulmonary sarcoidosis centers

## Timelines

- Interim safety data: December 2019
- Study completion: mid-2020<sup>(1)</sup>

## Possible Future Development

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

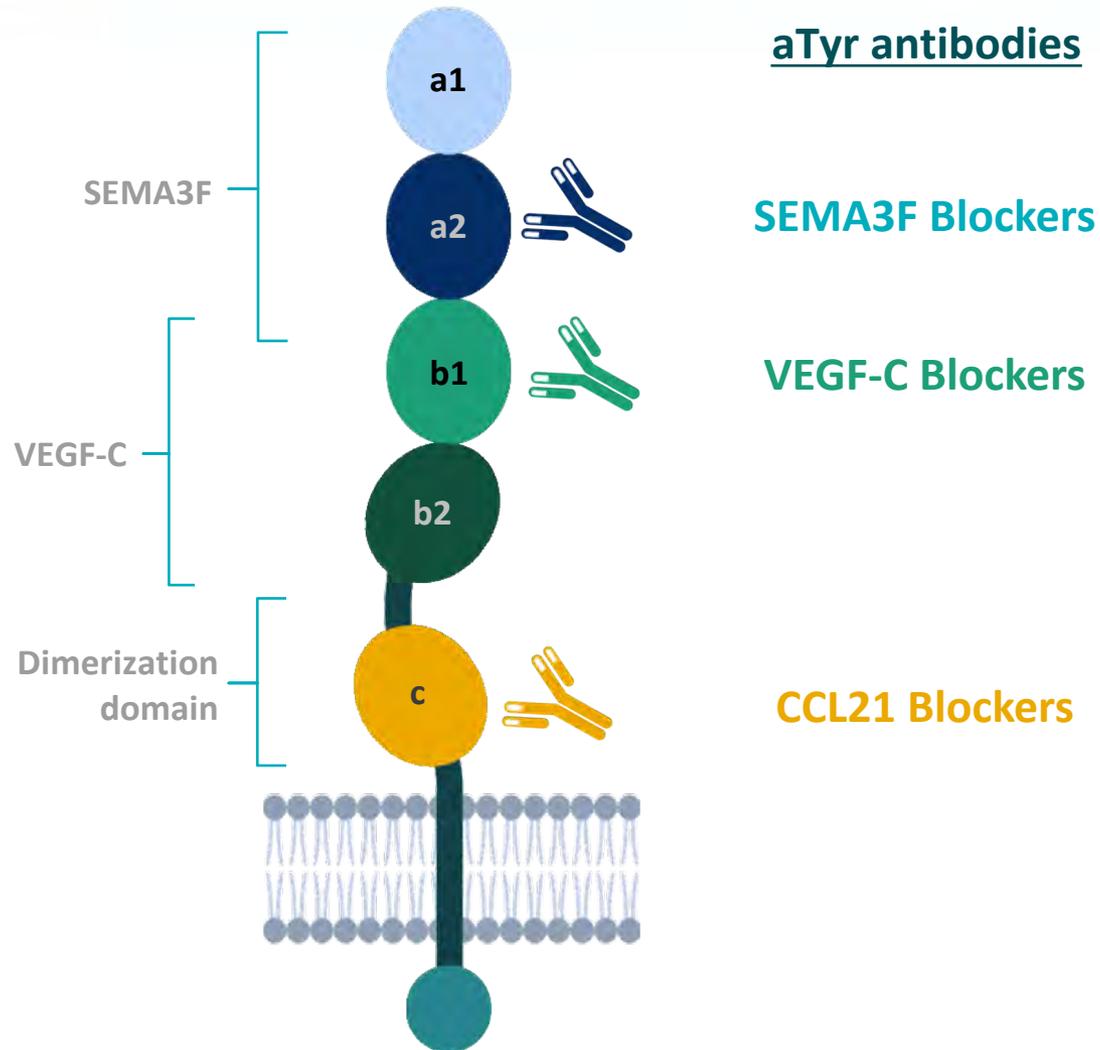


# NRP2 Biology

# NRP2: A Novel Therapeutic Target

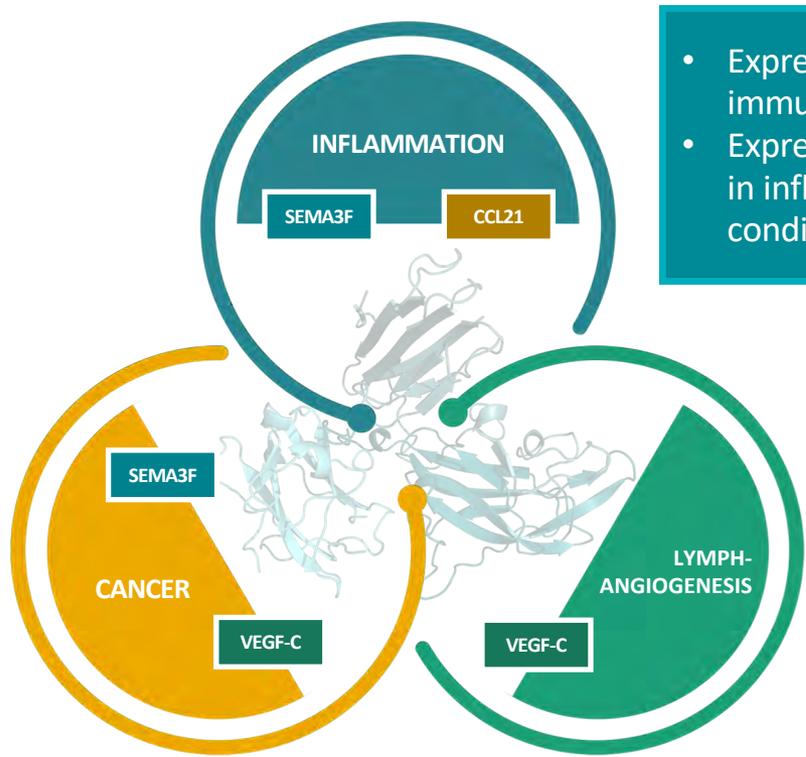
- NRP2 is a potentially novel target for cancer and inflammatory disorders
- Acts as a co-receptor for VEGF-C, class 3 Semaphorins and CCL21
- Expression is upregulated in tumors and immune cells during inflammation
- Expression is linked to worse outcomes in cancer
- aTyr has developed antibodies to selectively target different NRP2 epitopes for diverse therapeutic applications

# aTyr Human NRP2 Blocking Antibodies



# NRP2 is a Compelling Target for Cancer and Inflammation

- Overexpressed in a variety of cancers
- Tumor expression linked to worse outcomes



- Expressed on multiple immune cell types
- Expression upregulated in inflammatory conditions

- Lymphatic development and function impaired in NRP2 knockout



# aTyr Pharma

## Company Value Drivers

# Upcoming Catalysts

## **ATYR1923**

- Interim Phase 1b/2a safety data December 2019
- Phase 1b/2a results mid-2020<sup>(1)</sup>
- Potential expansion into Phase 2 studies for CHP and CTD-ILD

## **CSL R&D**

- aTyr eligible for up to \$17m in option fees
- Option granted to CSL to negotiate licenses for worldwide rights to each IND candidate that emerges from the collaboration

## **NRP2 Antibody Candidates**

- Potential new pipeline opportunities through academic and industry collaborations

# Building Value...for Patients and Shareholders

- ✓ Platform of new biology
  - ✓ tRNA synthetase biology
  - ✓ NRP2 antibody program
- ✓ Robust clinical program: ATYR1923
  - ✓ Understanding of MOA
  - ✓ Translational studies in multiple ILD models
  - ✓ Phase 1b/2a clinical study in pulmonary sarcoidosis
- ✓ Supported by top tier investors
- ✓ Cash, cash equivalents, and investment at \$38.1m as of 9/30/2019



Thank You