



A New Path to Medicine

Stifel 2019 Healthcare Conference

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November 20, 2019

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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⁽¹⁾
 - Interim safety data December 2019
 - Final results mid-2020⁽²⁾
- 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		CSL Behring			
NRP2 Candidates	Undisclosed					

Novel Functions of tRNA Synthetases

INTRACELLULAR

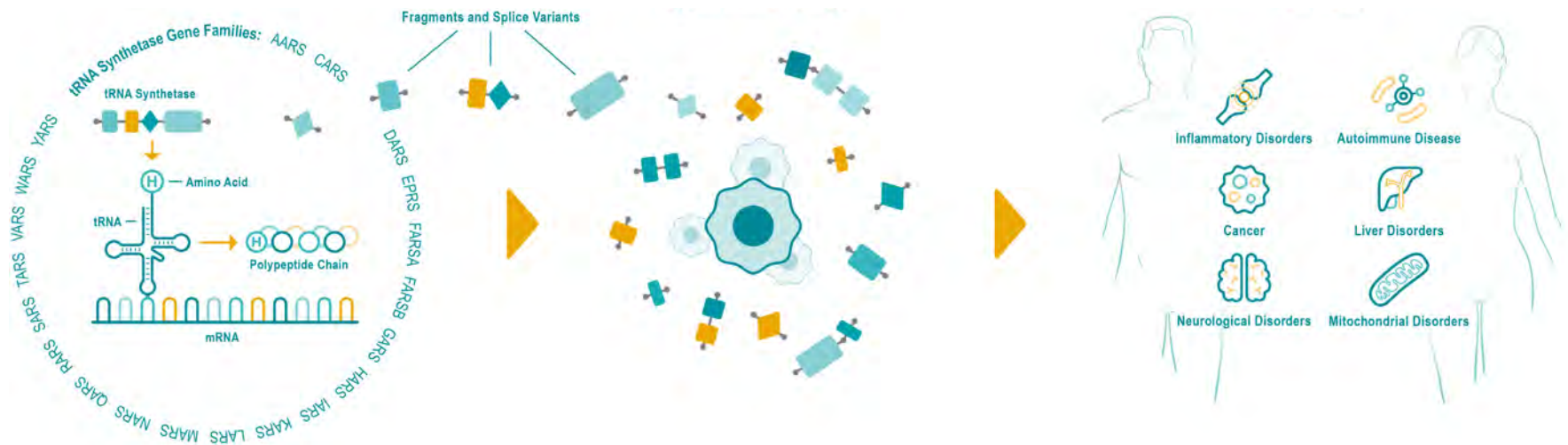
Catalyze Protein Synthesis

EXTRACELLULAR*

Secreted in Circulation and Tissue
to Regulate Diverse Pathways

PHYSIOLOGICAL

Pathway Disruption Associated
with Disease



CSL Behring Collaboration

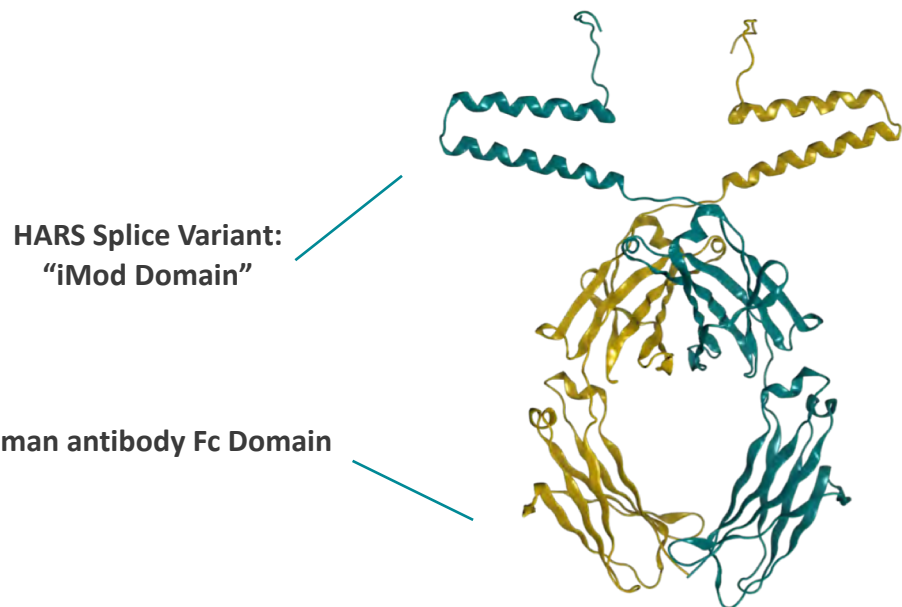
Goal	<ul style="list-style-type: none">• Identify new IND candidates from up to four tRNA synthetases from aTyr's proprietary pipeline of novel proteins (non-HARS derived)
Terms	<ul style="list-style-type: none">• CSL Behring to fund all R&D costs• aTyr eligible for up to \$17m in option fees if CSL 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 \$278k of collaboration revenue through Q3 2019



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

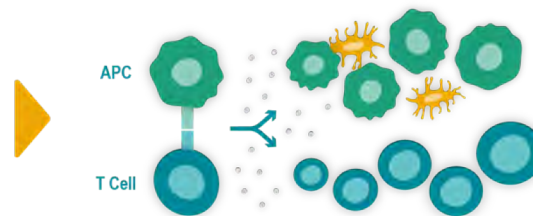
ATYR1923 Mechanism of Action in ILD

Disease Trigger



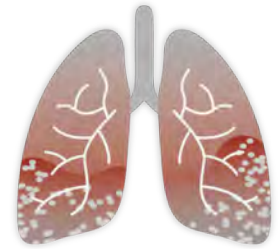
Organic; inorganic; infectious; autoimmune

Aberrant Immune Response



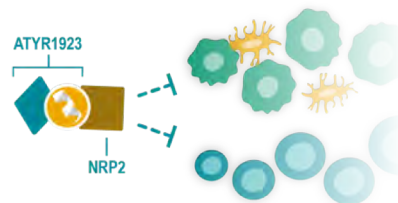
T-cell activation; pro-inflammatory cytokines/chemokines triggering fibrotic pathways; NRP2 upregulation on immune cells

Lung Inflammation & Fibrosis



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

ATYR1923 Dampens Immune Responses



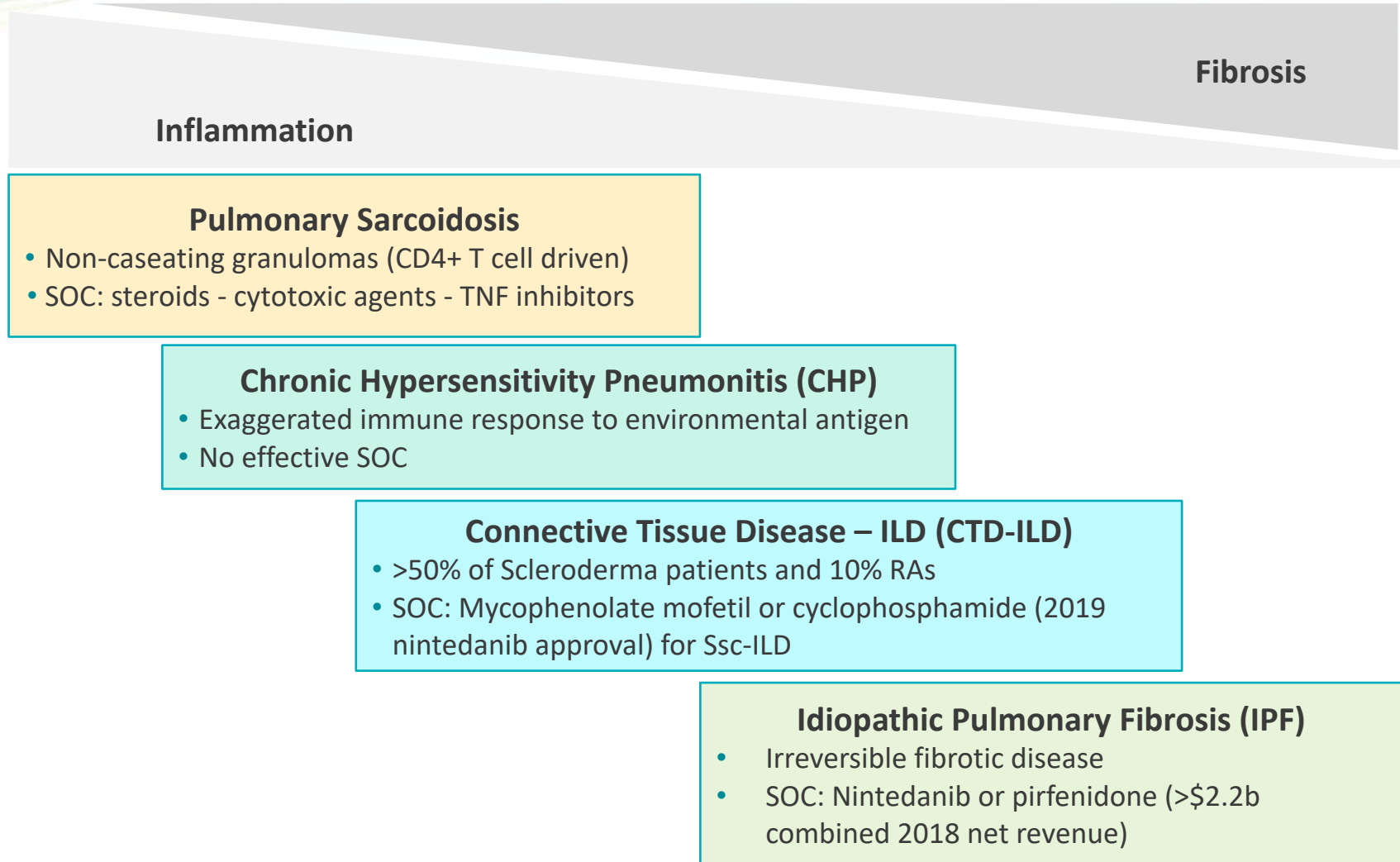
ATYR1923 binds to NRP2 and downregulates cytokine and chemokine production and T-cell activation

Stabilized Lung



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

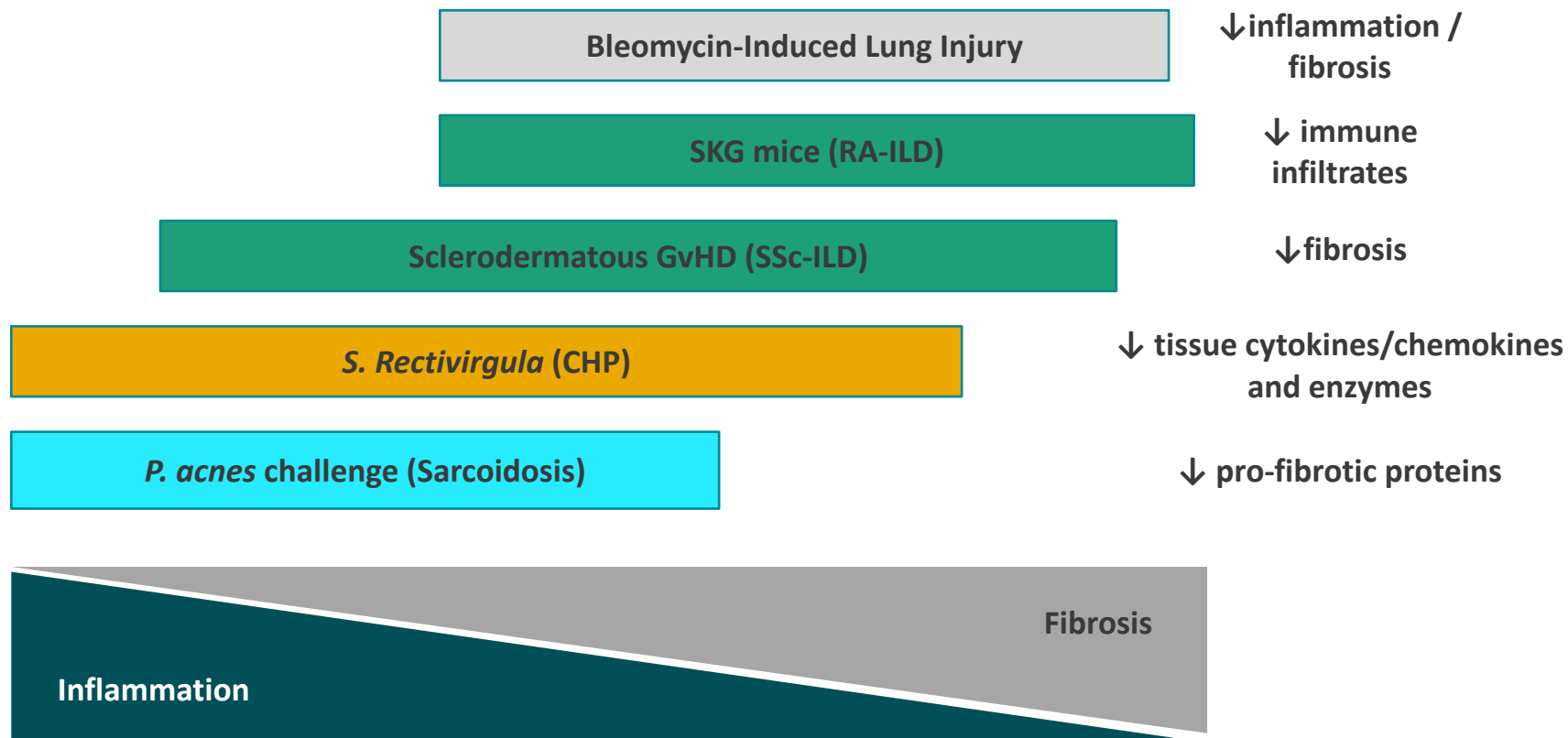
ILDs Share Persistent Immune Engagement



Pre-Clinical Translational Data Supports ILD Development

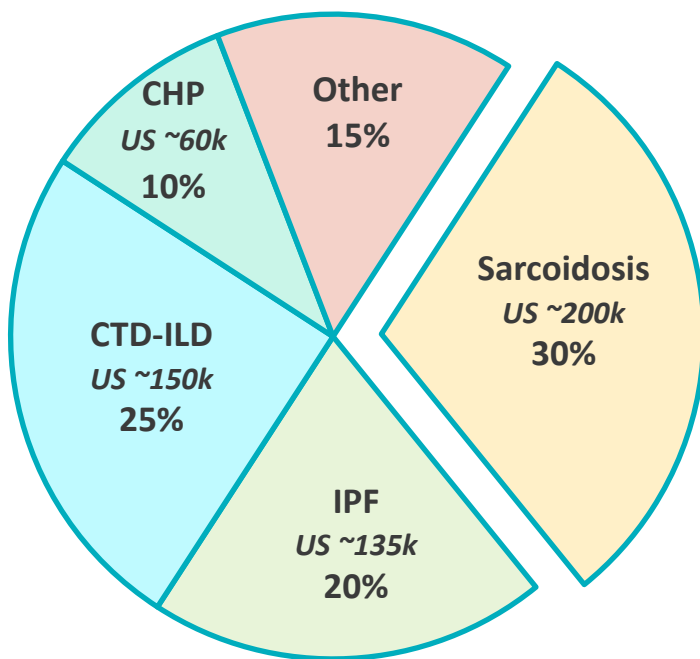
Bleomycin-Induced Lung Injury (IPF) – Mouse	<ul style="list-style-type: none">• ATYR1923 reduced fibrosis and inflammation• Comparator: pirfenidone• Presented at ATS, May 2017
Bleomycin-Induced Lung Injury (IPF) – Rat	<ul style="list-style-type: none">• ATYR1923 returned lung function to normal and reduced 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

Demonstrated Effect in Multiple ILD Models

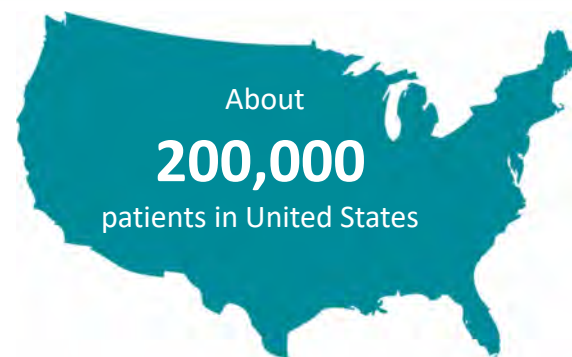


Sarcoidosis: A Major Form of ILD

ILD Patient Distribution



\$2-3b Global Opportunity⁽¹⁾



50% require systemic therapy



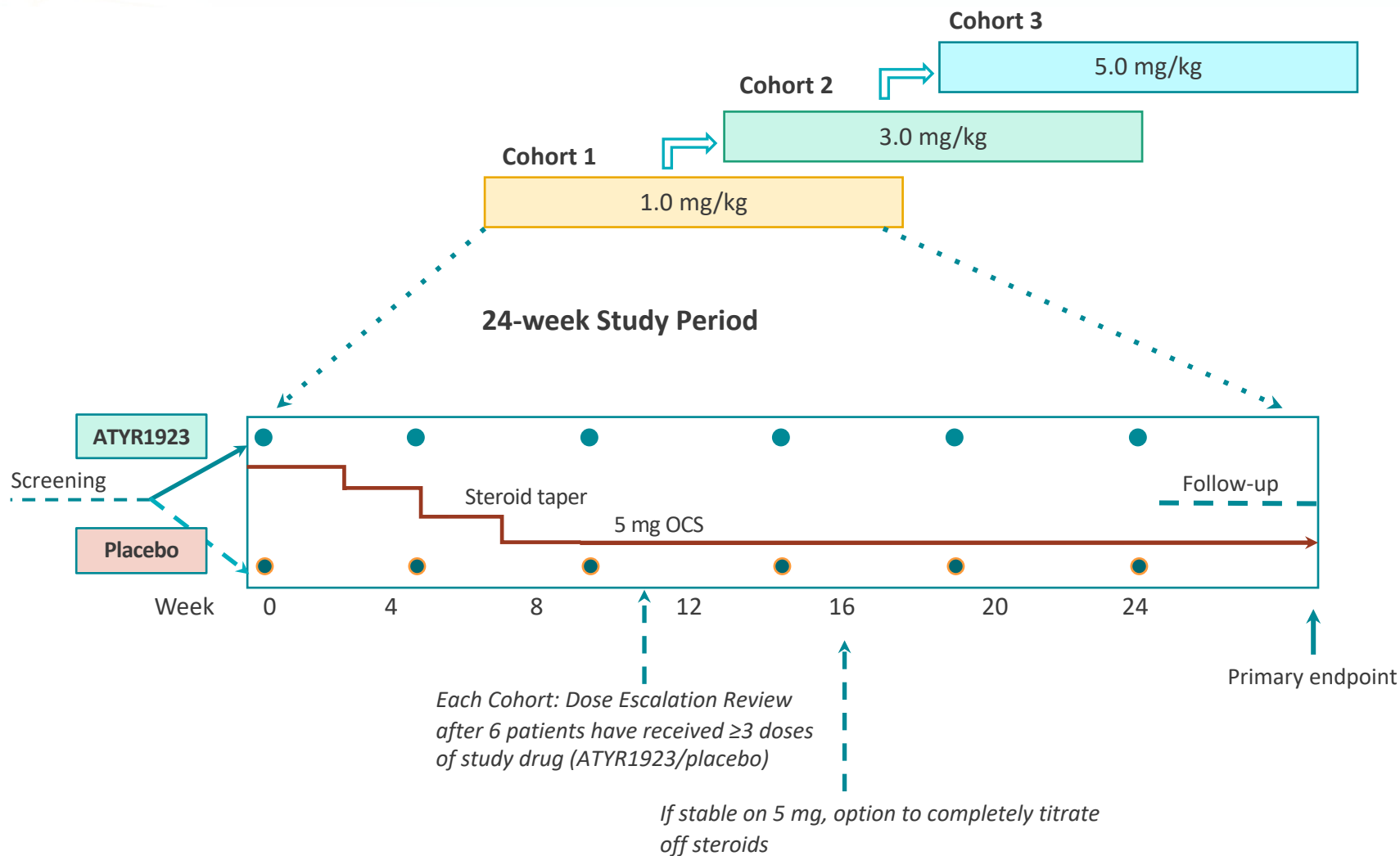
30% with chronic progressive disease despite currently available treatment



ATYR1923 Phase 1b/2a Study in Pulmonary Sarcoidosis

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 5.0 mg by week 8— by week 16, if stable, option to completely titrate off steroids
Endpoints	<ul style="list-style-type: none">• Primary<ul style="list-style-type: none">◦ Safety and tolerability of multiple ascending IV ATYR1923 doses• Secondary<ul style="list-style-type: none">◦ 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	<ul style="list-style-type: none">• Phase 1 in 36 healthy volunteers complete• Patient enrollment ongoing in Phase 1b/2a in ~15 leading pulmonary sarcoidosis centers
Timelines	<ul style="list-style-type: none">• Interim safety data: December 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)

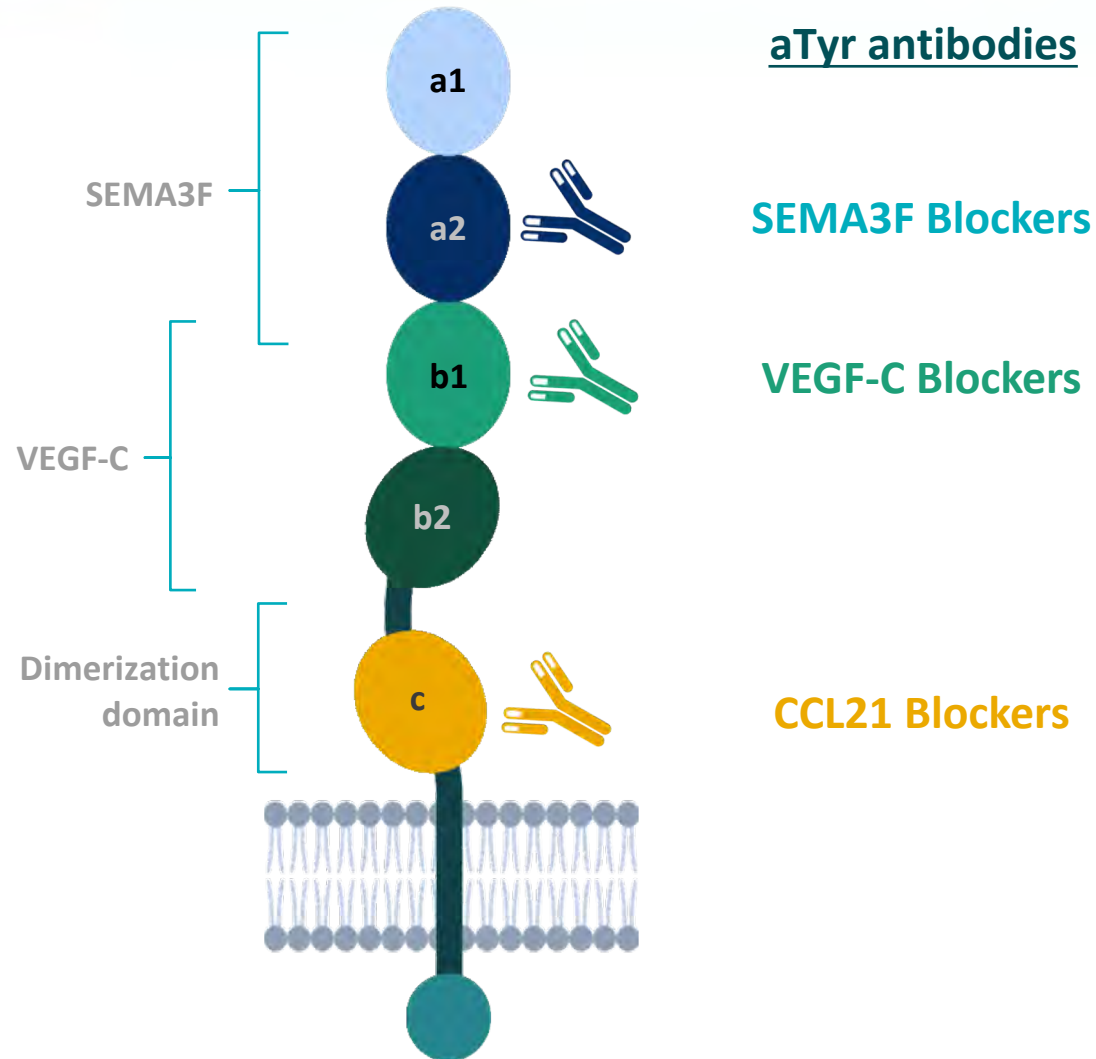


NRP2 Biology

NRP2: A Novel Therapeutic Target

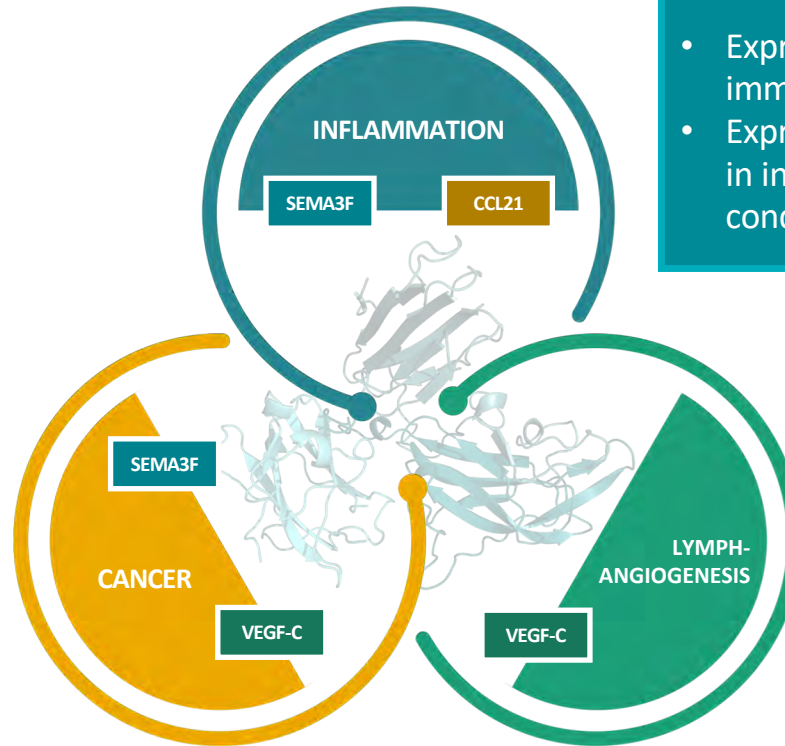
- NRP2 is a potentially novel target for cancer and inflammatory disorders
- Acts as a co-receptor for VEGF-C, class 3 Semaphorins and CCL21
- Expression is upregulated in tumors and immune cells during inflammation
- Expression is linked to worse outcomes in cancer
- aTyr has developed antibodies to 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⁽¹⁾
- ❑ 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