



A New Path to Medicine

H.C. Wainwright & Co. Global Investment Conference

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Forward Looking Statements

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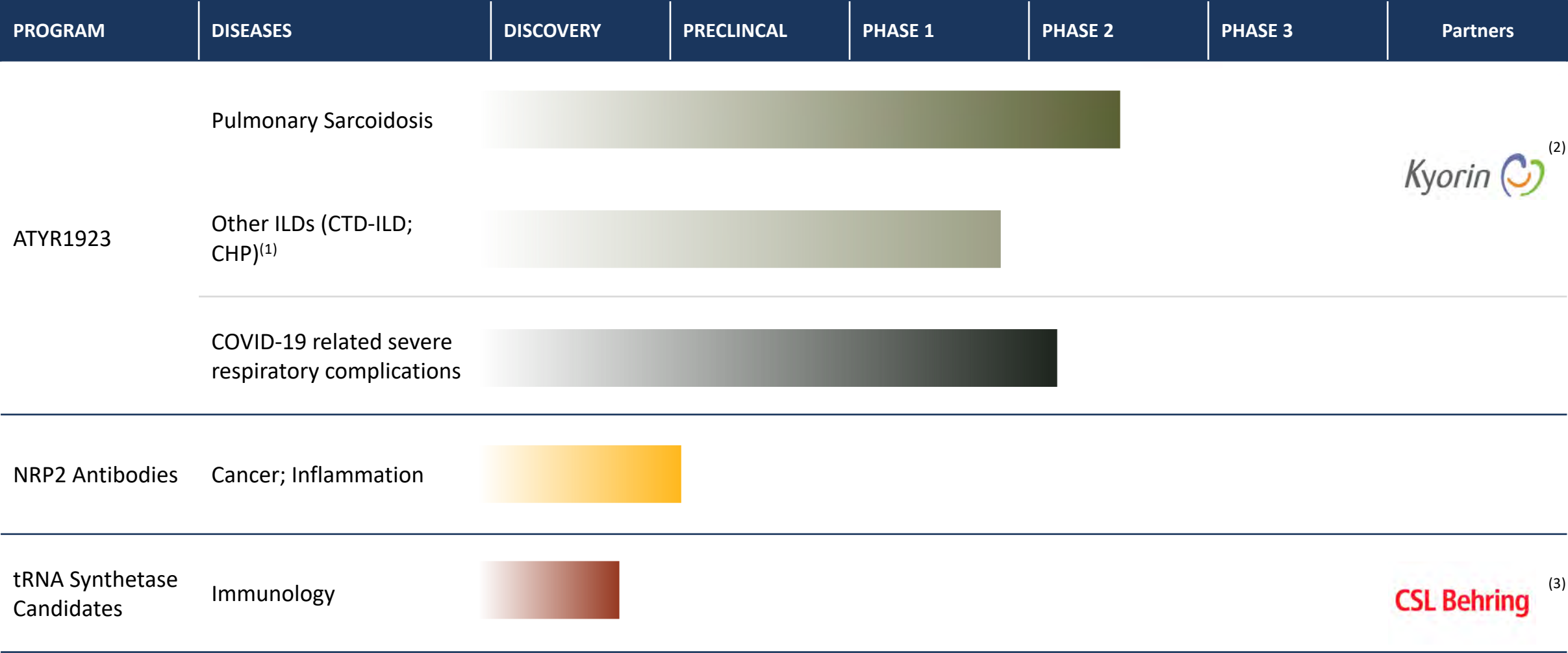
aTyr: A New Path to Medicine

Mission	• Develop a new class of medicines based on proprietary biology platform
Phase 2 clinical program: ATYR1923	• Potential first-in-class immunomodulator for severe inflammatory lung diseases • Phase 1b/2a study in pulmonary sarcoidosis⁽¹⁾ • Phase 2 study in COVID-19 related severe respiratory complications readout expected in Q4 2020⁽²⁾ • Japanese Phase 1 healthy volunteer study initiated by Kyorin Pharmaceuticals in Q3 2020
Pipeline of novel discovery candidates	• First anti-neuropilin-2 (NRP2) antibody IND candidate expected to be announced in Q4 2020 • tRNA synthetase immunology research collaboration update anticipated in Q4 2020
Financial Position	• Cash, cash equivalents and investments at \$41.4m as of June 30, 2020

(1) Timing dependent on impact of the COVID-19 pandemic

(2) Timing dependent on site initiation and patient enrollment

aTyr Development Pipeline



4

(1)

CTD-ILD = connective tissue disease-related ILD; CHP = chronic hypersensitivity pneumonitis

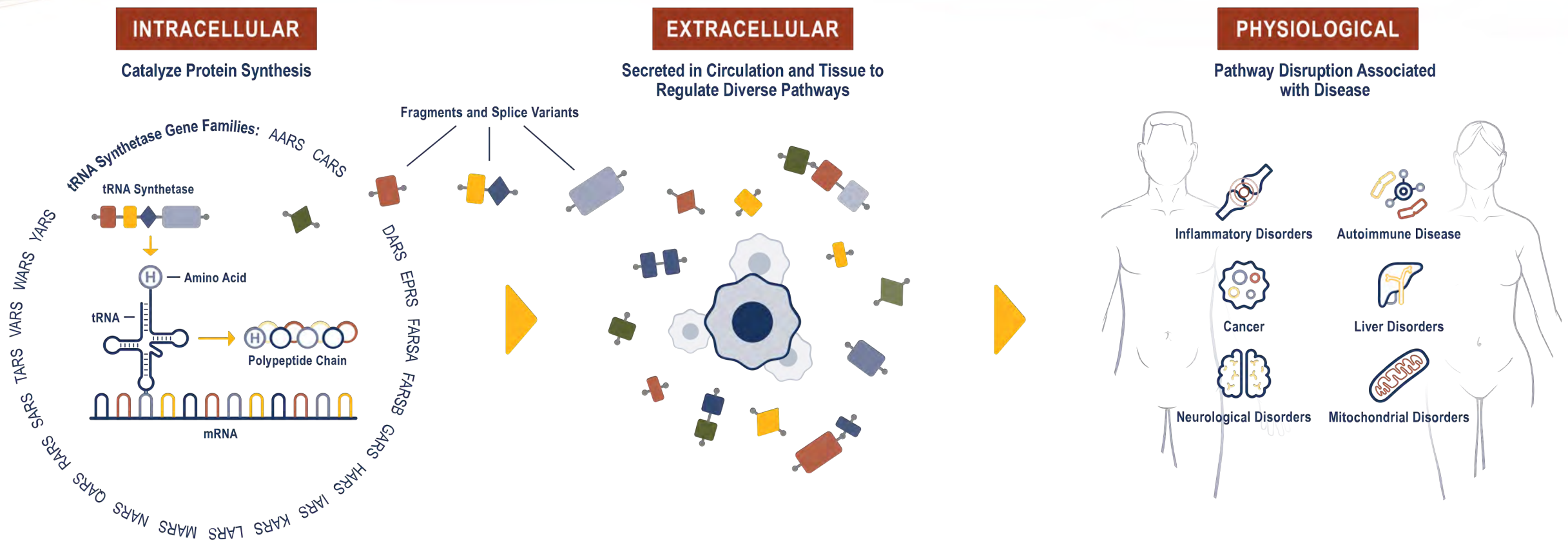
(2)

Kyorin partnership for ILD in Japan

(3)

CSL partnership for up to 4 tRNA synthetases

tRNA Synthetases May Have Novel Functions Extracellularly



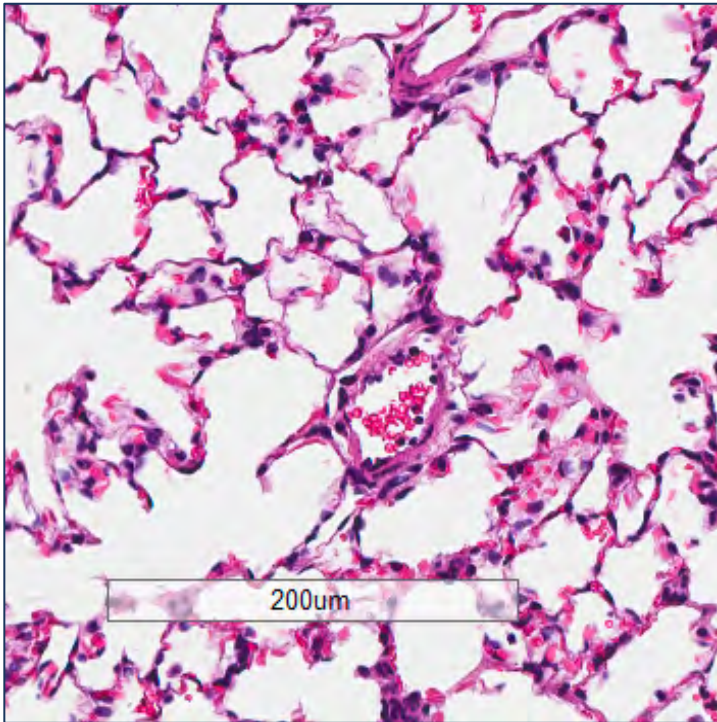


ATYR1923

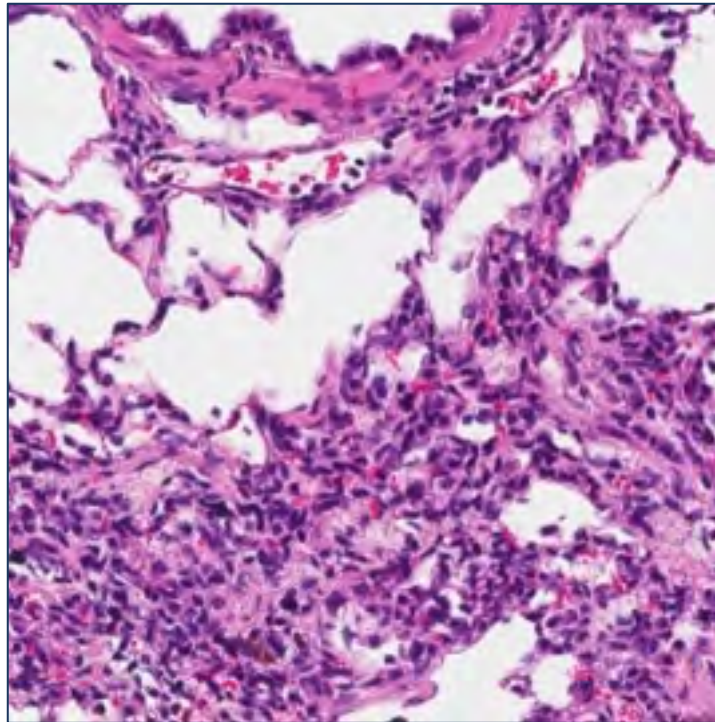
A Novel Immunomodulator for Inflammatory Lung Disease

A Novel Mechanism to Treat Inflammation

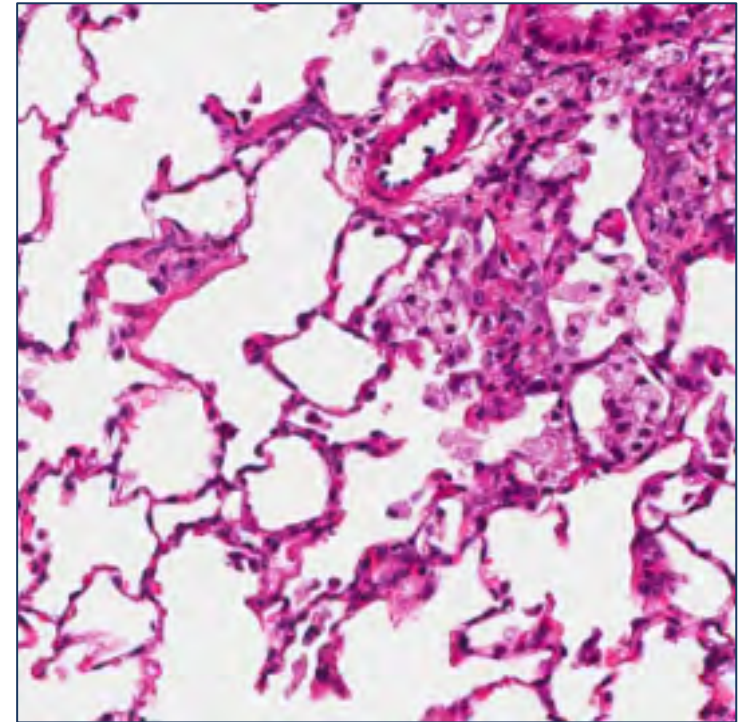
Healthy lung



Injured lung



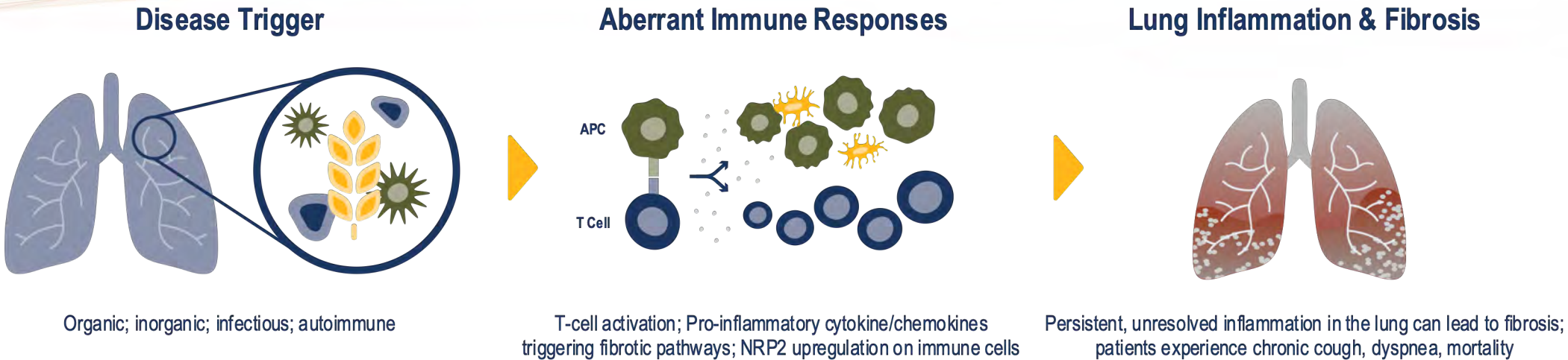
ATYR1923 treated



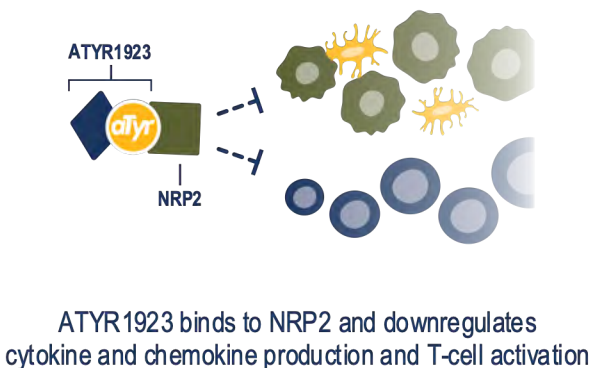
ATYR1923: Potential First-in-Class Therapy for Severe Inflammatory Lung Disease

- Fc fusion protein therapeutic derived from aTyr's proprietary protein library
- Binds selectively to NRP2, a cell surface receptor upregulated in inflamed lung tissue
- Downregulates inflammatory and pro-fibrotic cytokine and chemokine levels as well as histological inflammation and fibrosis in pre-clinical models
- Well tolerated in 25 healthy subjects in Phase 1 with PK supporting monthly IV Dosing
- No safety concerns identified in independent interim safety reviews in pulmonary sarcoidosis and COVID-19 patients

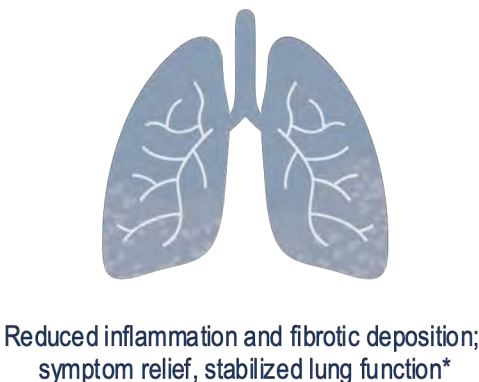
ATYR1923 Mechanism of Action in Inflammatory Lung Disease



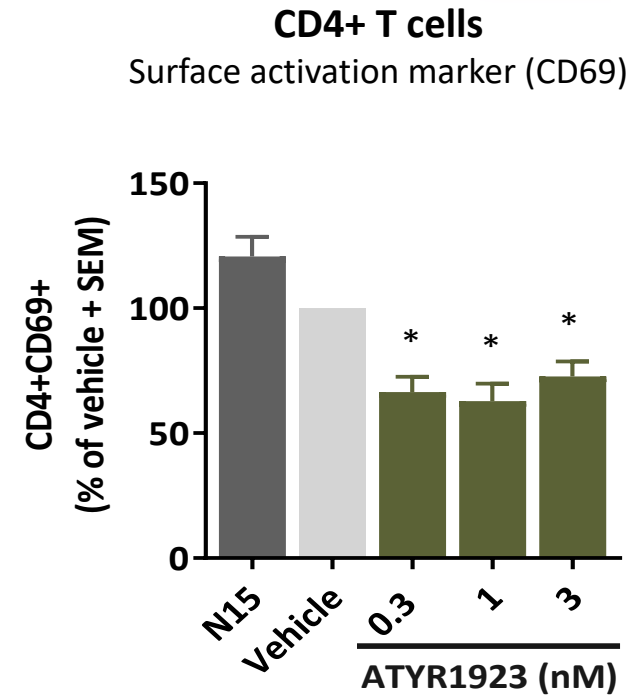
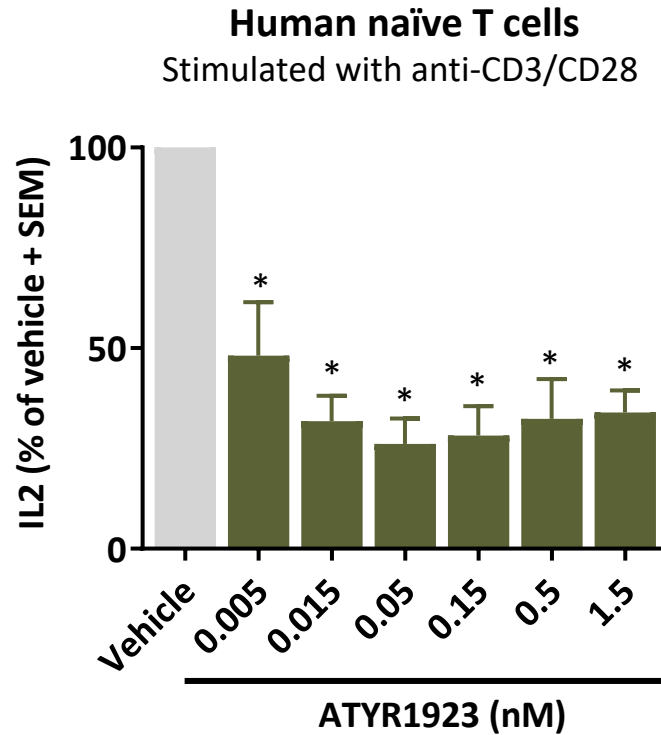
ATYR1923 Dampens Immune Responses



Stabilized Lung

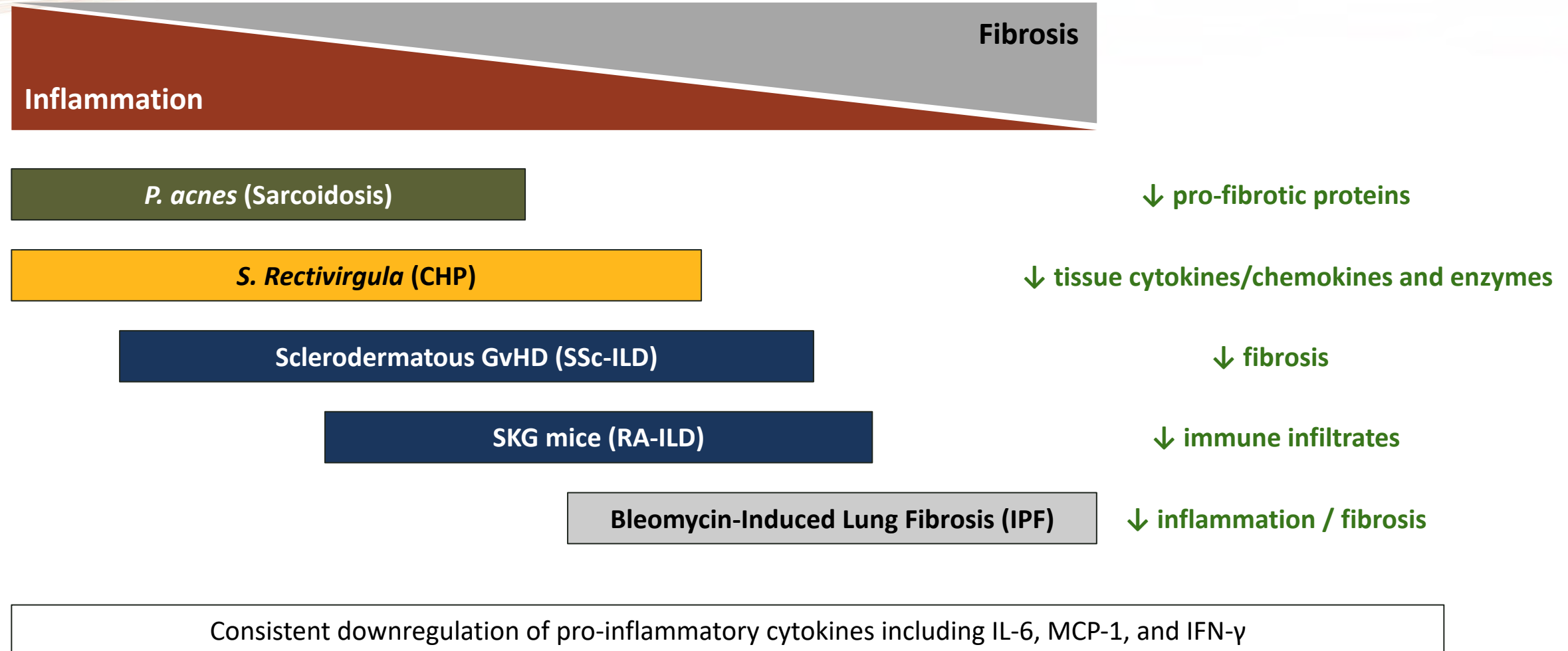


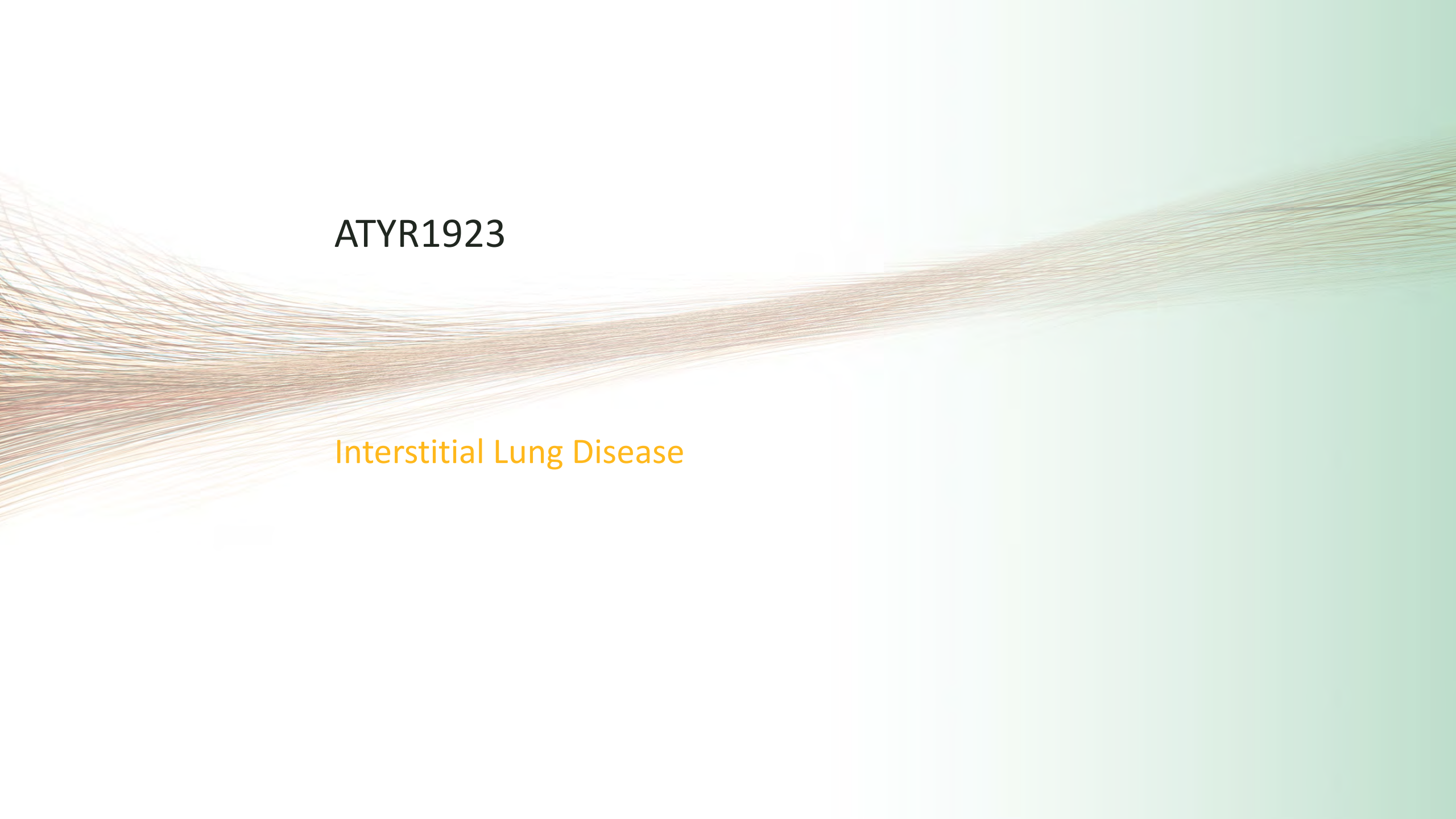
First Identified Mechanism: Inhibition of T Cell Activation



Also inhibits release of other cytokines: IFN γ , IL-17, IL-5, IL-13, IL-21, IL-10, TNF α

Demonstrated Effect in Animal Lung Injury Models

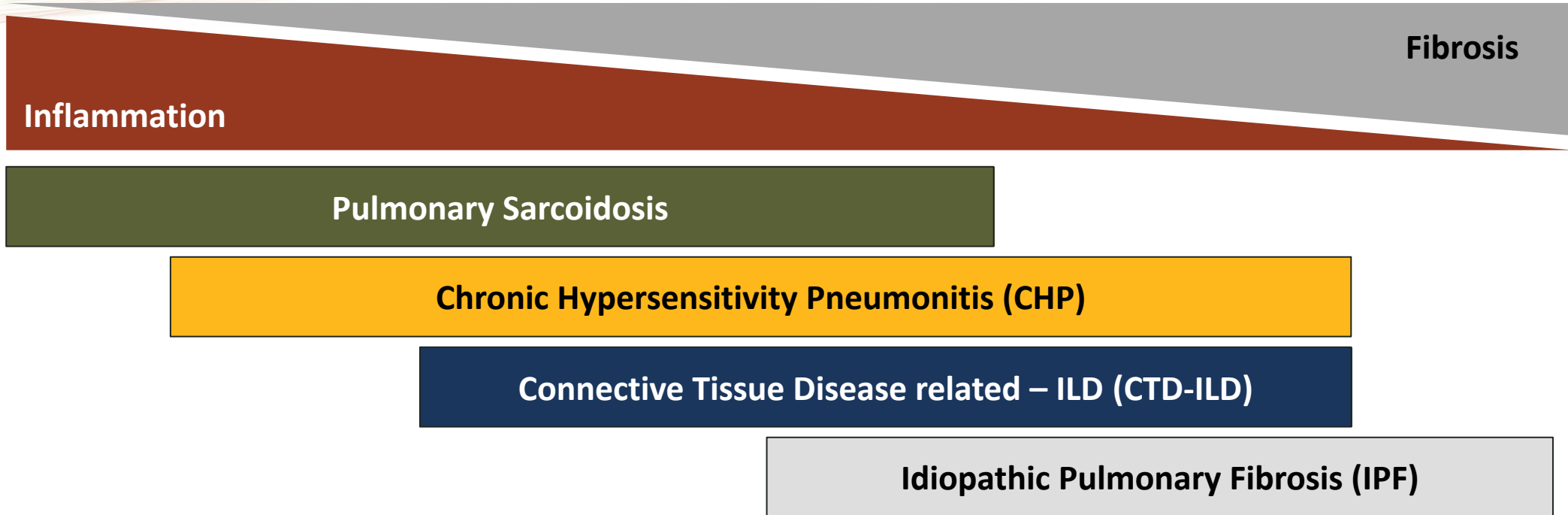




ATYR1923

Interstitial Lung Disease

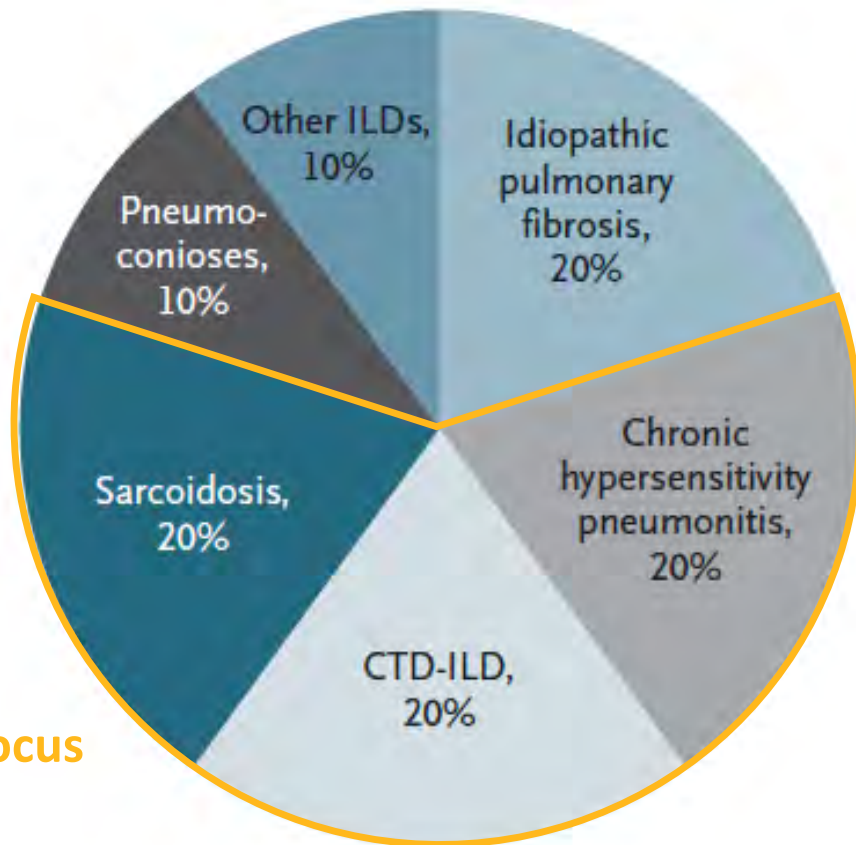
ILDs Share Common Immune Pathology Leading to Fibrosis



- ILDs lie on a spectrum of inflammation and fibrosis, but all share an immune pathology
- Progression to fibrosis is a key driver of morbidity and mortality
- By targeting aberrant immune response driving fibrosis, ATYR1923 has potential to improve outcomes in multiple ILDs

Market Opportunity in Inflammatory Interstitial Lung Disease

Relative Distribution of ILDs in the USA⁽¹⁾



aTyr focus

- >200 types of ILD: 4 major types comprise 80% of patients
- Limited standard of care with substantial morbidity and mortality
- aTyr focused on 3 most inflammatory types: ~500-600k US patients⁽²⁾; ~3m globally
- \$2-3b global market opportunity⁽³⁾

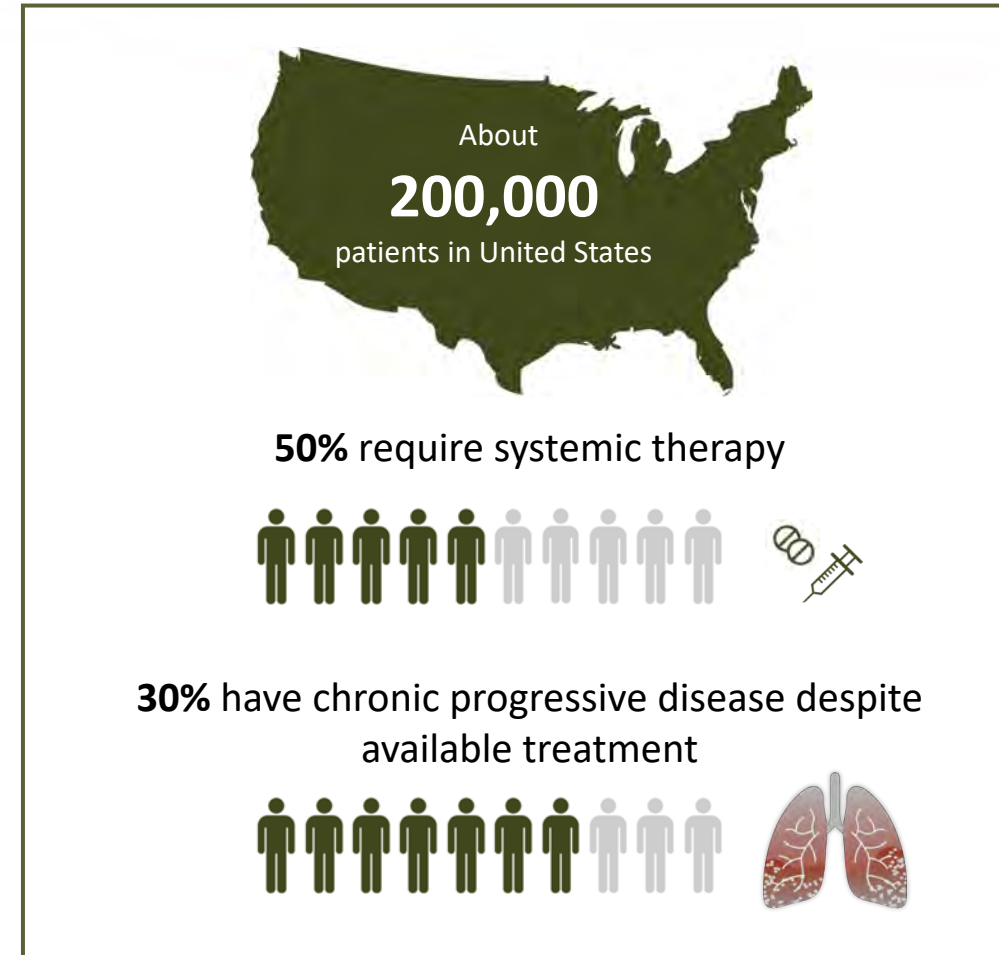
(1) Lederer, Martinez. NEJM 2018

(2) All ILDs individually have potential for orphan status

(3) aTyr estimates for ATYR1923 in Pulmonary Sarcoidosis, CHP, CTD-ILD; excludes IPF

First ATYR1923 Indication: Pulmonary Sarcoidosis

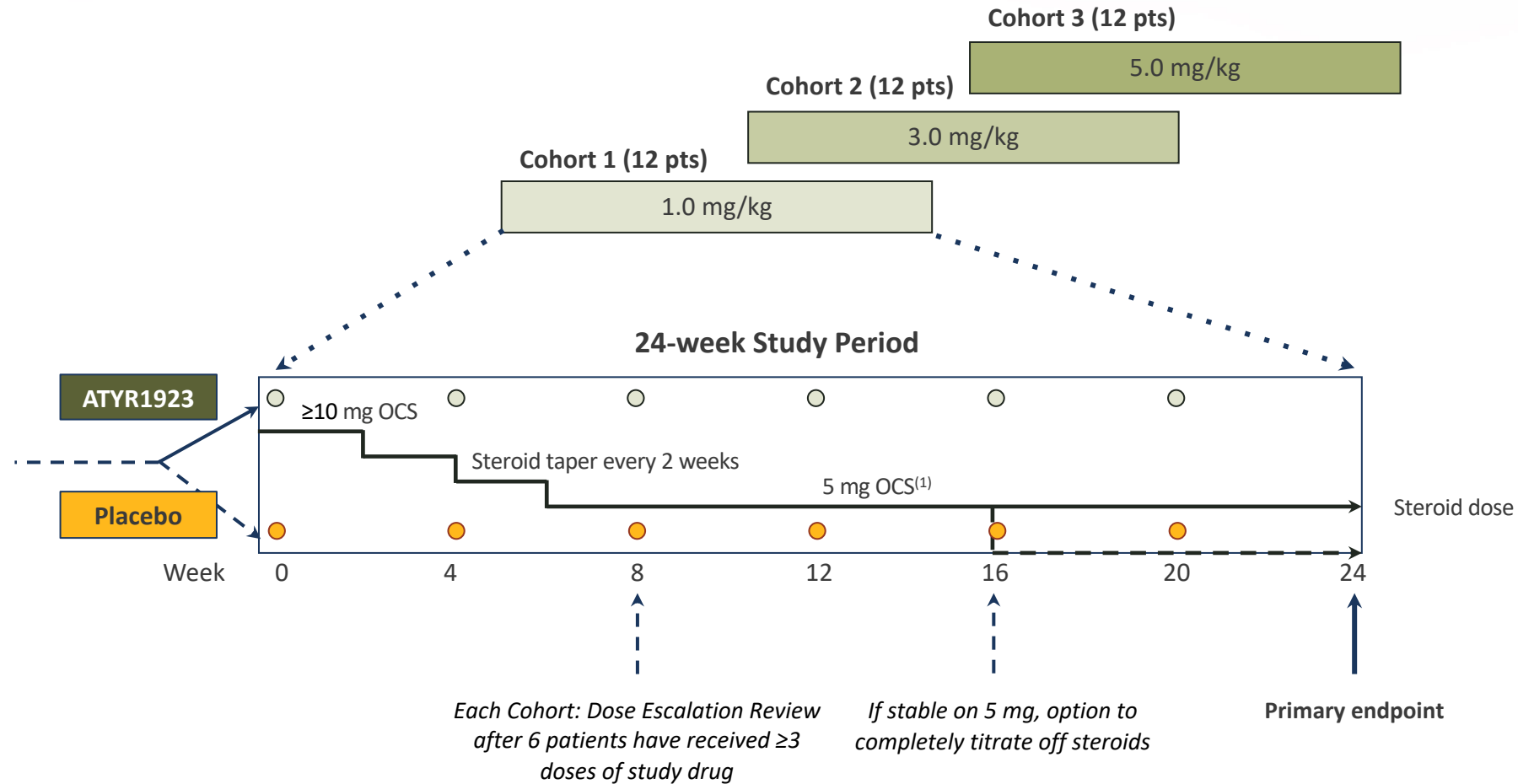
- Inflammatory disease of unknown etiology characterized by the formation of granulomas (clumps of immune cells)
- T cell driven: CD4+ (Th1 / Th17)
- Pulmonary sarcoidosis occurs in ~90% of all sarcoidosis patients
- Treatment options are limited with associated toxicity: Corticosteroids, antimetabolite immunosuppressants, TNF inhibitors



Phase 1b/2a Study in Pulmonary Sarcoidosis Ongoing

Design	• Randomized (2:1), double-blind, placebo-controlled, multiple ascending dose • 3 IV doses of ATYR1923 being tested at 1, 3, and 5mg/kg • Forced steroid taper to 5 mg by week 8; taper to 0 mg possible at week 16 in responders
Population	• 36 histologically confirmed pulmonary sarcoidosis patients • ≥ 10 mg stable oral corticosteroid treatment • Symptomatic/active disease at baseline
Primary Endpoint	• Safety and tolerability of multiple ascending IV ATYR1923 doses
Secondary Endpoints	• 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 Pulmonary Sarcoidosis Study Schema



ATYR1923 Japan Collaboration

Kyorin Overview

- Founded: 1923
- Focus: Respiratory, ENT, Urology
- 1600 employees: incl. 350 in R&D; 750 sales reps covering top respiratory centers in Japan
- Sales: ~\$1b USD
- Market cap: \$1.1b USD (4569:JP TSE)

Key Terms

- Scope: ATYR1923; Japan; ILD
- Upfront payment: \$8m
- Development, regulatory and commercial milestones: \$167m
- Tiered sales royalties into double digits
- Kyorin to fund all development and commercial activities in Japan

Phase 1 study to evaluate the safety, pharmacokinetics and immunogenicity in Japanese healthy volunteers initiated.

ATYR1923

COVID-19 Related Severe Respiratory Complications

ATYR1923 for COVID-19 Related Severe Respiratory Complications

COVID-19 Pathology	ATYR1923 MOA
• A subset of COVID-19 patients experience significant lung inflammation leading to morbidity and mortality • Lung inflammation is driven by certain cytokines: IL-2, -7, -6,-10, G-CSF, MCP1, MIP1A and TNF-α	• ATYR1923 decreases inflammatory cytokine release, including IL-2, TNF-α, and IL-13, from human T cells activated <i>in vitro</i> • ATYR1923 anti-inflammatory and anti-fibrotic effects, including decreased cytokine/chemokine signaling (IL-6, MCP1 and IFN-γ), have been demonstrated in multiple animal models of immune-mediated lung injury
• Lung tissue from patients who died from COVID-19 related respiratory failure shows increased NRP2 ⁽¹⁾ • SARS-CoV-2 Spike protein S1 directly binds to the b1 domain of NRP2 ^{(2) (3)}	• ATYR1923 binds selectively to NRP2, primarily in the b1 domain

(1) Ackermann, M., Verleden, S.E., Kuehnel, M., et al. NEJM 2020.

(2) <http://doi.org/dx5d>; 2020

(3) <http://doi.org/dx5c>; 2020

ATYR1923 Phase 2 Study in COVID-19 Related Severe Respiratory Complications Ongoing

Objective	Evaluate safety and preliminary efficacy of ATYR1923 in subjects hospitalized with COVID-19-related severe respiratory complications not requiring mechanical ventilation
Design	Randomized, double-blind, placebo controlled, single dose
Population	30 adult patients with severe respiratory complications related to COVID-19 infection
Doses	Randomized 1:1:1 - Single dose of 1.0 or 3.0 mg/kg ATYR1923 or Placebo
Endpoints	• Primary: Safety and Tolerability • Secondary: Oxygenation, Fever, Hospital / ICU metrics, Inflammatory markers



NRP2 Antibodies

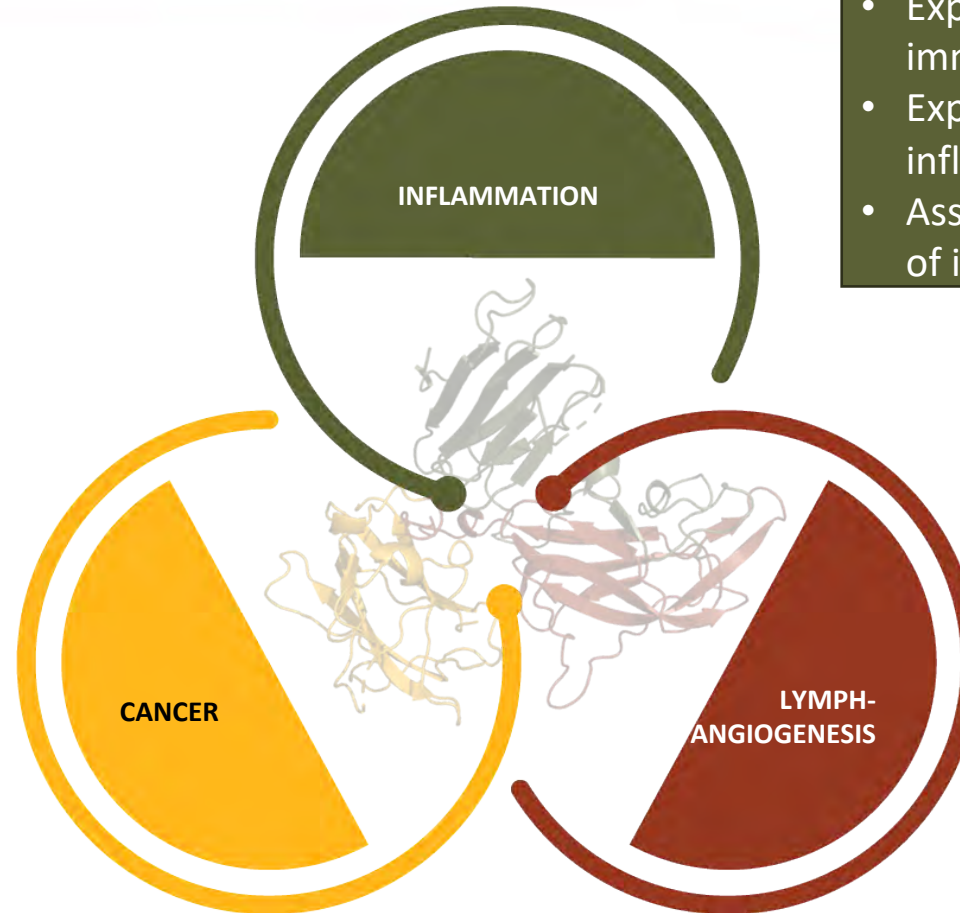
Regulating Diverse Disease Pathways

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
- NRP2 expression is upregulated on tumors and immune cells during inflammation
- NRP2 expression is linked to worse outcomes in many cancers
- aTyr has developed antibodies to selectively target different NRP2 epitopes for diverse therapeutic applications
- aTyr's aNRP210 antibody blocked VEGF-C binding to NRP2 and showed tumor inhibitory effect in preclinical models of triple-negative breast cancer, increasing sensitivity to chemotherapy ⁽¹⁾
- This data suggests aNRP210 could potentially be effective in certain types of solid tumors, including aggressive tumors ⁽¹⁾

NRP2 is a Compelling Target for Cancer and Inflammation

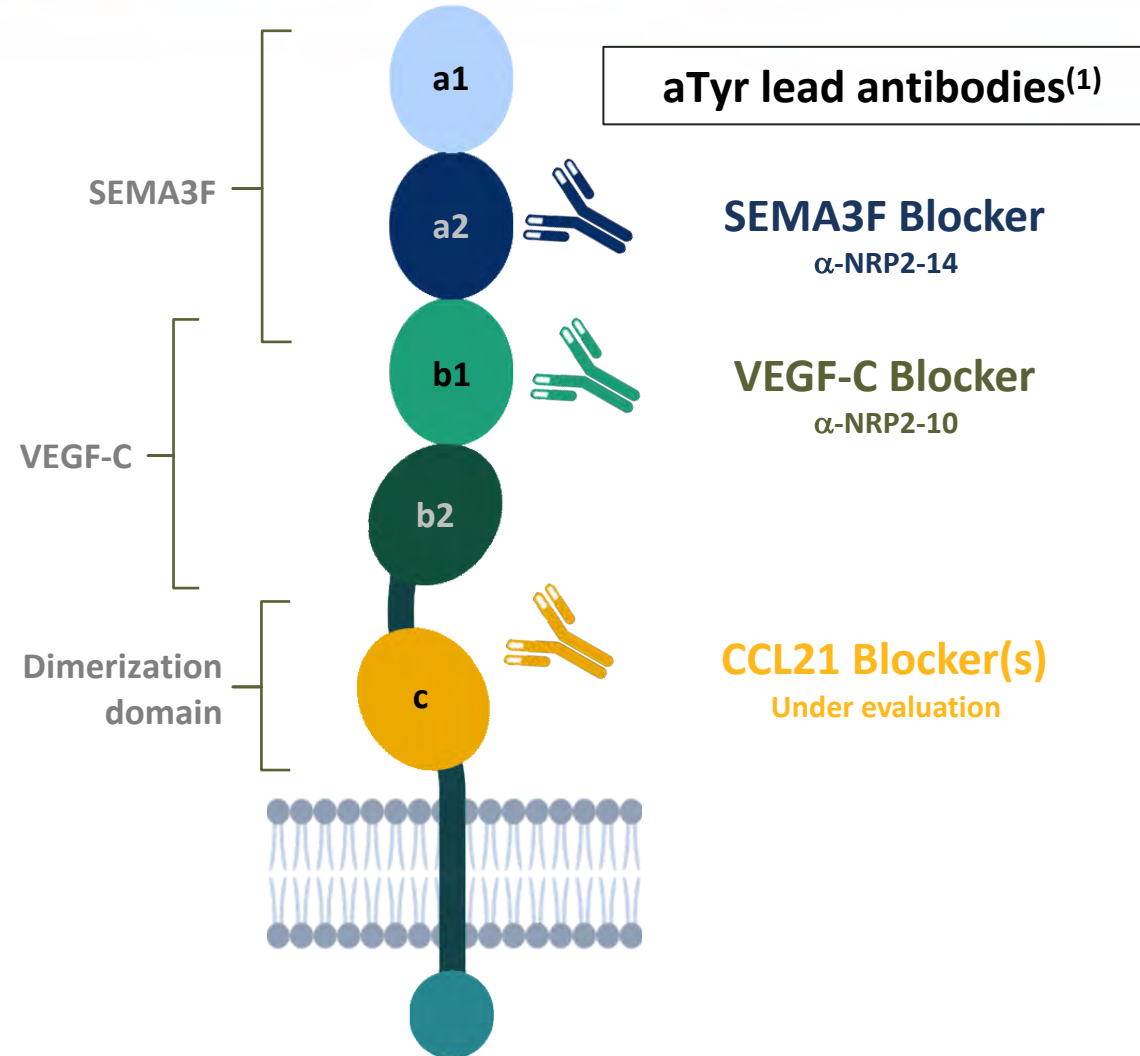
- Overexpressed in a variety of cancers
- Tumor expression linked to worse outcomes



- Expressed on multiple immune cell types
- Expression upregulated in inflammatory conditions
- Associated with trafficking of immune cells

- Lymphatic development and function impaired in NRP2 knockout

aTyr is Developing Human NRP2 Blocking Antibodies





tRNA Synthetases

A Potential New Therapeutic Protein Class

tRNA Synthetases: A Potential New Therapeutic Protein Class

- aTyr owns IP covering proteins derived from all 20 tRNA synthetase gene families
- Lead program ATYR1923 is based on a naturally occurring splice variant of one of these families, histidyl-tRNA synthetase (HARS)
- tRNA synthetases are secreted extracellularly and occur in novel forms which lose their canonical function
- Extracellular tRNA synthetase disruption (genetic / autoimmune) is associated with disease in humans
- aTyr working with leading biopharmaceutical company CSL Behring on identifying new IND candidates for immunological disorders in up to four tRNA synthetases from aTyr's pipeline (non-HARS derived)
 - CSL will fund all R&D activities and will pay a total of up to \$17.0 million in option fees if all four synthetase programs advance
 - aTyr will grant CSL an option to negotiate licenses for worldwide rights to each IND candidate that emerges from this research collaboration



A New Path to Medicine

aTyr: A New Path to Medicine

- Platform of proprietary new biology
- Phase 2 clinical program: ATYR1923
 - Novel MOA for inflammatory lung disease
 - Demonstrated effect in multiple animal lung injury models
 - Phase 1 in healthy volunteers completed
 - Phase 1b/2a clinical study in pulmonary sarcoidosis enrolling in US – positive interim safety data reported 12/2019
 - Kyorin collaboration for ILD in Japan with total deal value up to \$175m; Phase 1 study initiated
 - Phase 2 trial in COVID-19 patients with severe respiratory complications enrolling in US– positive outcome from interim safety analysis conducted by an independent data and safety monitoring board reported 8/2020
- Discovery stage programs in cancer and immunology
 - Recently published poster shows aTyr antibody anti-tumor effects in triple-negative breast cancer model
- Cash, cash equivalents, and investments at \$41.4m as of June 30, 2020

Upcoming Catalysts

ATYR1923

- Phase 1b/2a results in pulmonary sarcoidosis patients⁽¹⁾
 - Kyorin's Phase 1 in healthy volunteers to support trials for ILD in Japan initiated in Q3 2020
 - Phase 2 results in COVID-19 patients expected in Q4 2020⁽²⁾
 - Potential expansion into Phase 2 studies for second ILD indication
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NRP2 Antibodies

- Selection of first anti-NRP2 antibody IND candidate expected in Q4 2020
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tRNA Synthetase Candidates

- Outcome from the first phase of the CSL Behring research collaboration planned in Q4 2020
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⁽¹⁾ Timing dependent on impact of the COVID-19 pandemic
⁽²⁾ Timing dependent on site initiation and patient enrollment



Thank You