



A New Path to Medicine

February 2021

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

ATYR1923

- Immunomodulator for severe inflammatory lung diseases
- Pulmonary sarcoidosis trial enrollment completed – data expected Q3 2021
- Positive topline data reported January 2021 in COVID-19 pts

NRP2 Antibodies

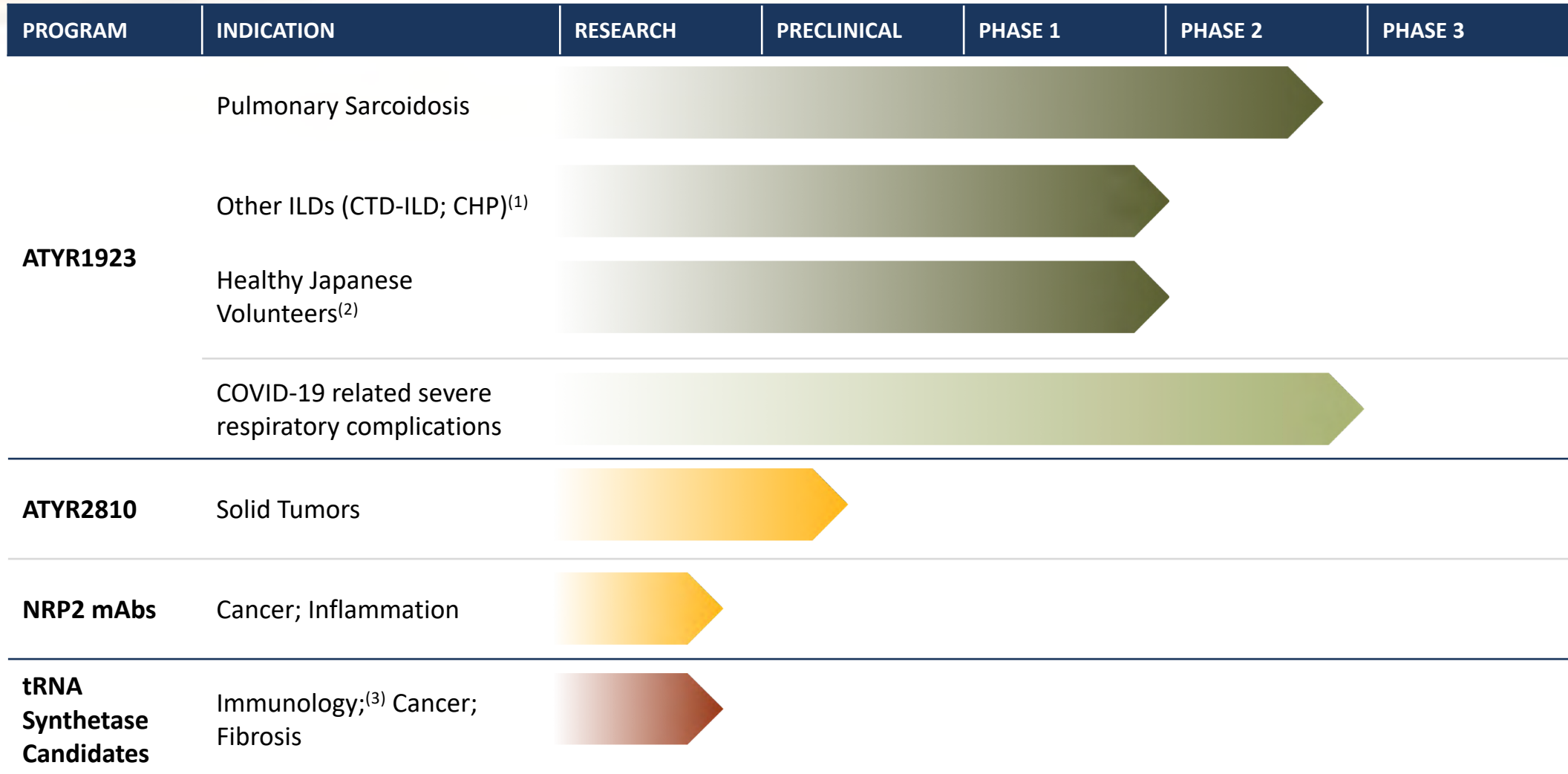
- ATYR2810: first anti-neuropilin-2 (NRP2) antibody for cancer – IND-enabling activities initiated
- NRP2 antibody research program for distinct therapeutic applications

Extracellular tRNA Synthetases

- IP portfolio covering protein derivatives from all 20 tRNA synthetase gene families
- Receptors identified for two new tRNA synthetases from our pipeline
- Discovery programs targeting cancer and NK cell biology

Financials: Cash, cash equivalents and investments at \$36.1m as of September 30, 2020

aTyr Development Pipeline

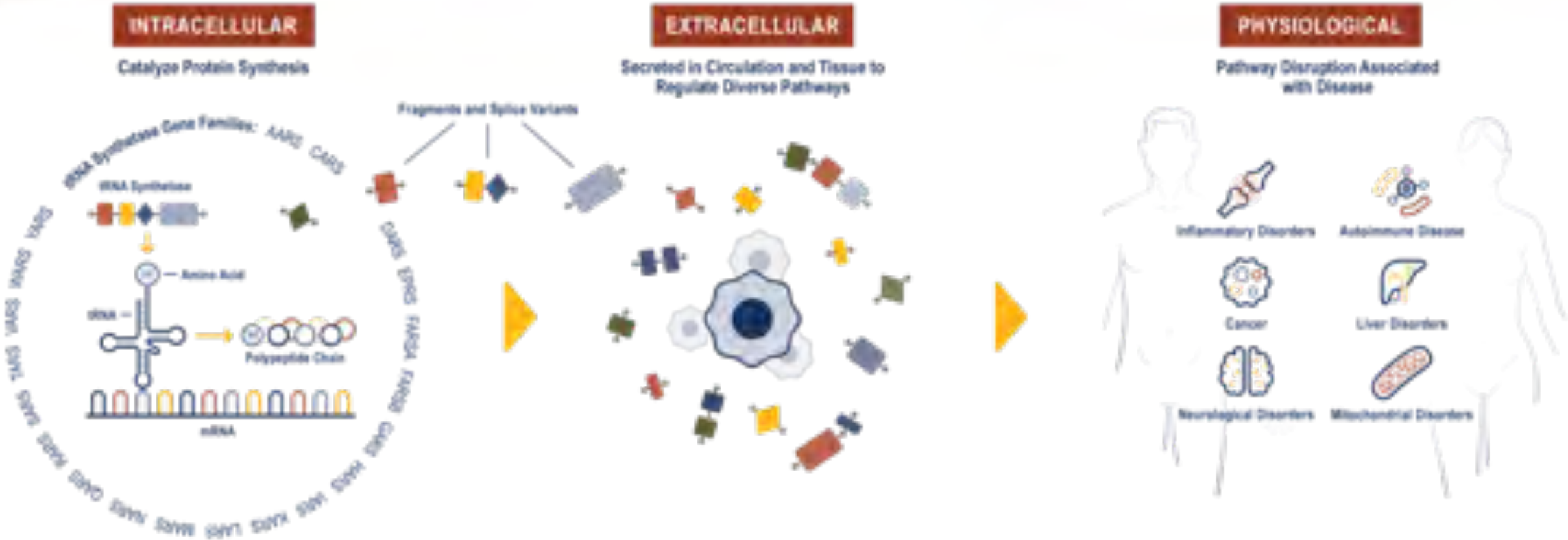


(1) CTD-ILD: connective tissue disease-related ILD (e.g. Scleroderma-related ILD); CHP: chronic hypersensitivity pneumonitis

(2) In partnership with Kyorin Pharmaceutical Co., Ltd.

(3) Includes research collaboration with CSL Behring, Ltd.

tRNA Synthetases May Have Novel Functions Extracellularly



The background of the slide is a blurred landscape featuring rolling hills and a body of water, with a color palette transitioning from light green on the left to a pale yellow on the right.

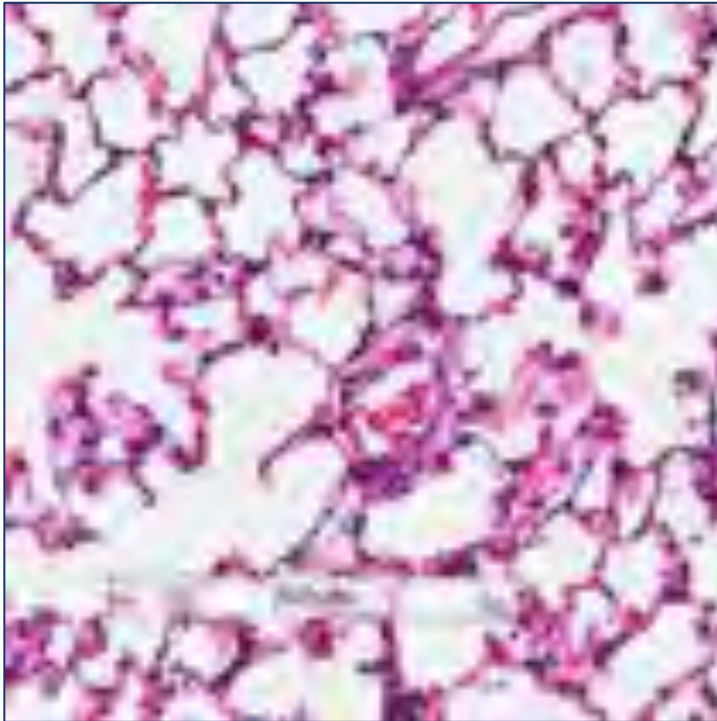
aTyr

ATYR1923

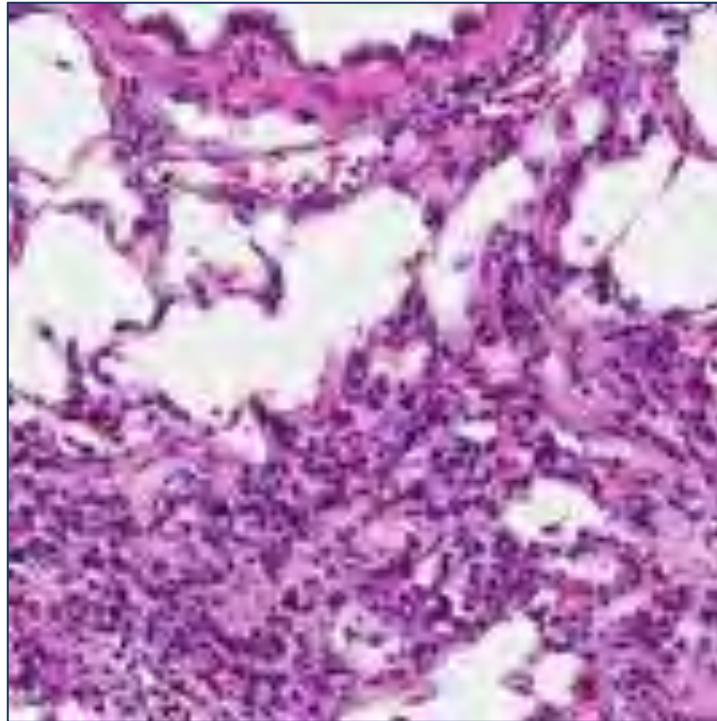
A Novel Immunomodulator for Inflammatory Lung Disease

A Novel Mechanism to Treat Inflammation

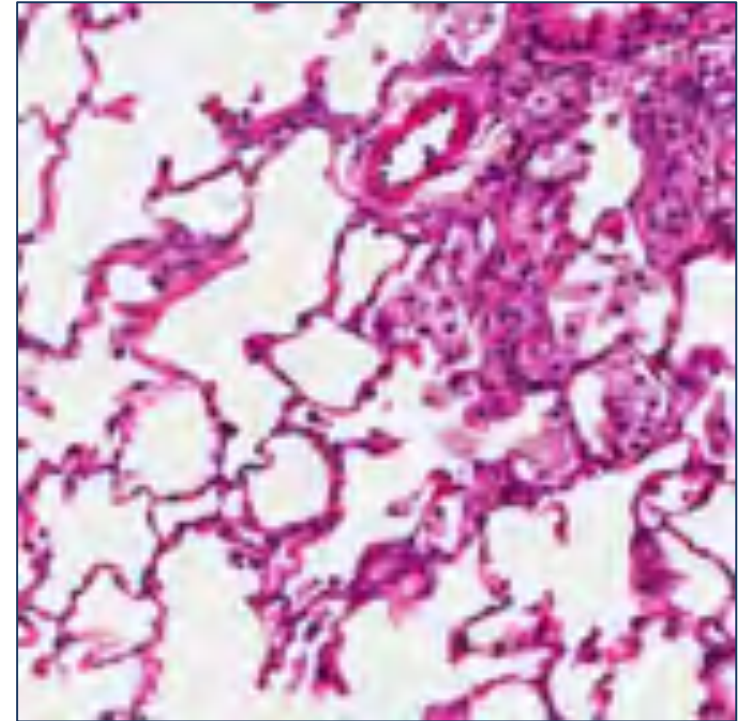
Healthy lung



Injured lung



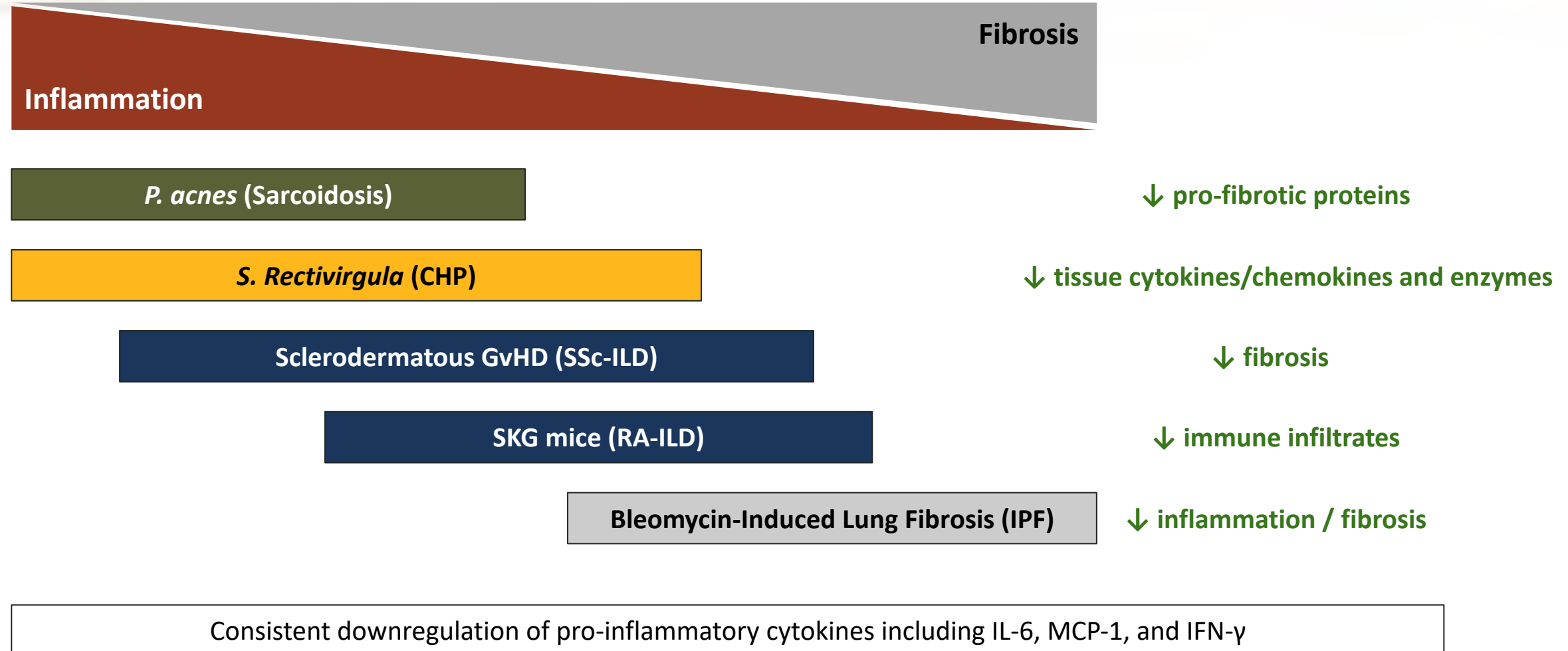
ATYR1923 treated



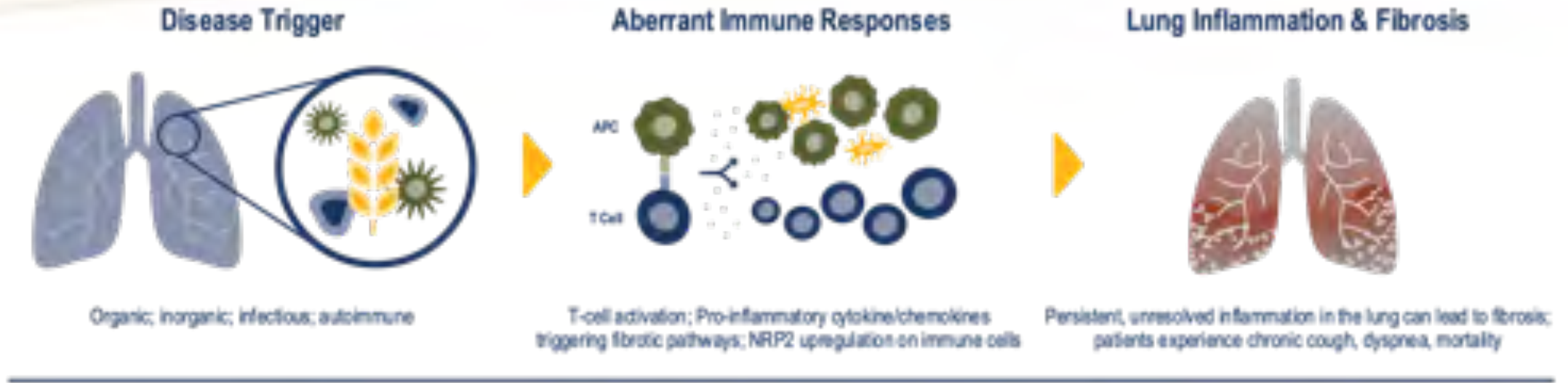
ATYR1923: Early Data Supports Therapeutic Potential in Immune-Mediated Lung Disease

- Fc fusion protein, based on lung-enriched histidyl-tRNA synthetase (HARS) fragment, recombinantly expressed in *E. coli*
- Receptor screen identified selective binding to NRP2, a cell surface receptor upregulated on key immune cells during inflammation and is enriched in inflamed lung tissue
 - NRP2 expression is detected in granulomas associated with human sarcoidosis of the lung and skin
 - Lung tissue from patients who died from COVID-19 related respiratory failure shows increased NRP2
- Downregulates inflammatory and pro-fibrotic cytokine and chemokine levels as well as histological inflammation and fibrosis in pre-clinical models
- Phase 1 study in healthy volunteers PK supports with once-monthly intravenous dosing
- Well tolerated in patients and subjects dosed to date with exposure up to 24 weeks

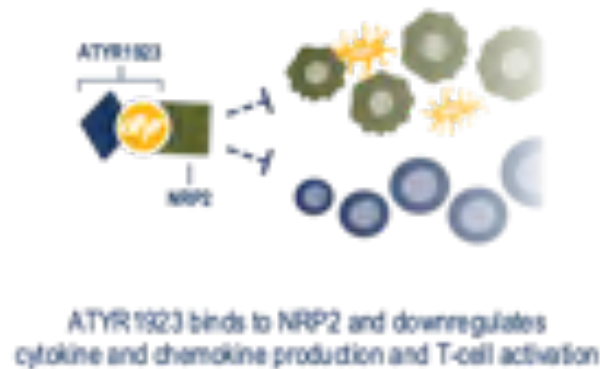
Demonstrated Effect in Animal Lung Injury Models



ATYR1923 Mechanism of Action in Inflammatory Lung Disease



ATYR1923 Dampens Immune Responses



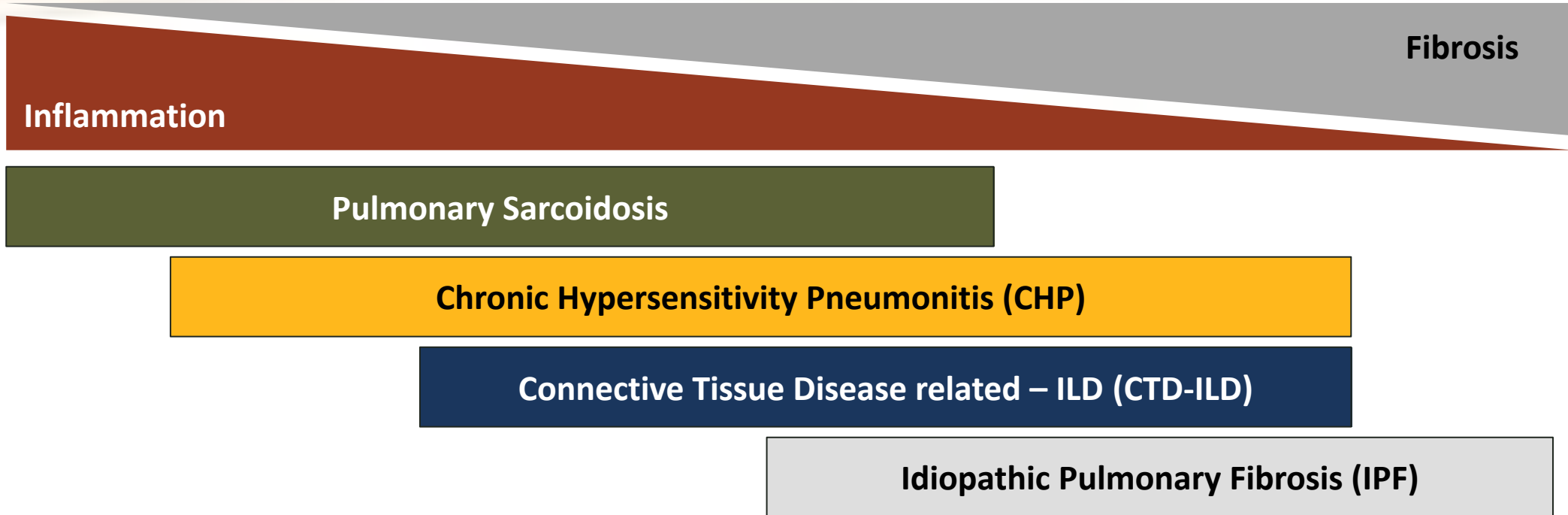
Stabilized Lung



ATYR1923

Interstitial Lung Disease

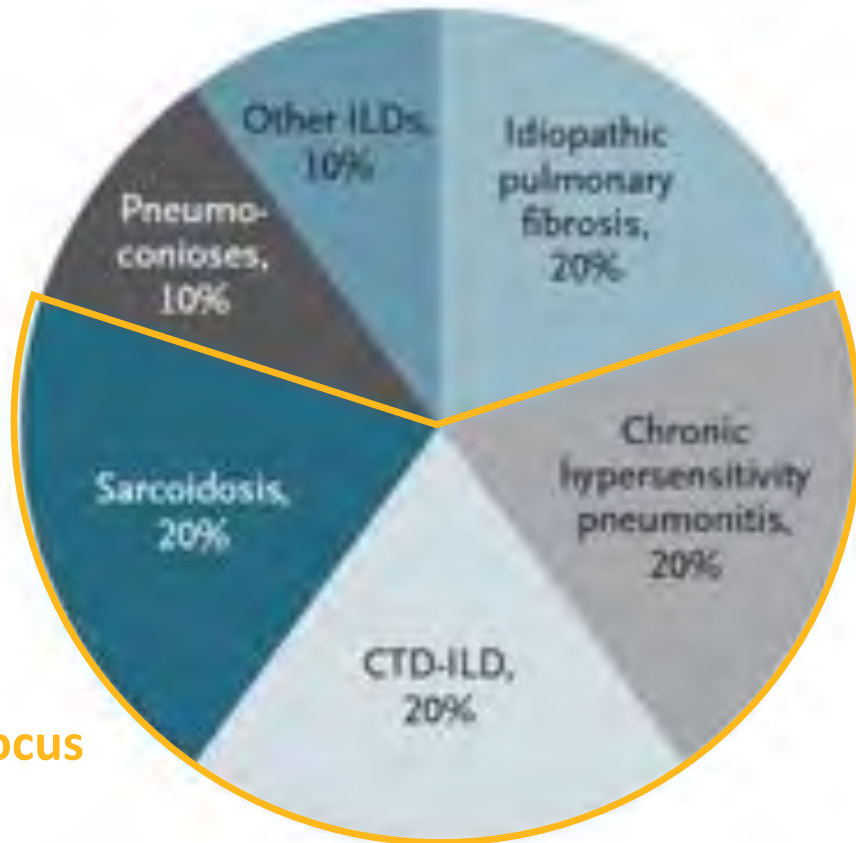
ILDs Share Common Immune Pathology Leading to Fibrosis



- 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⁾

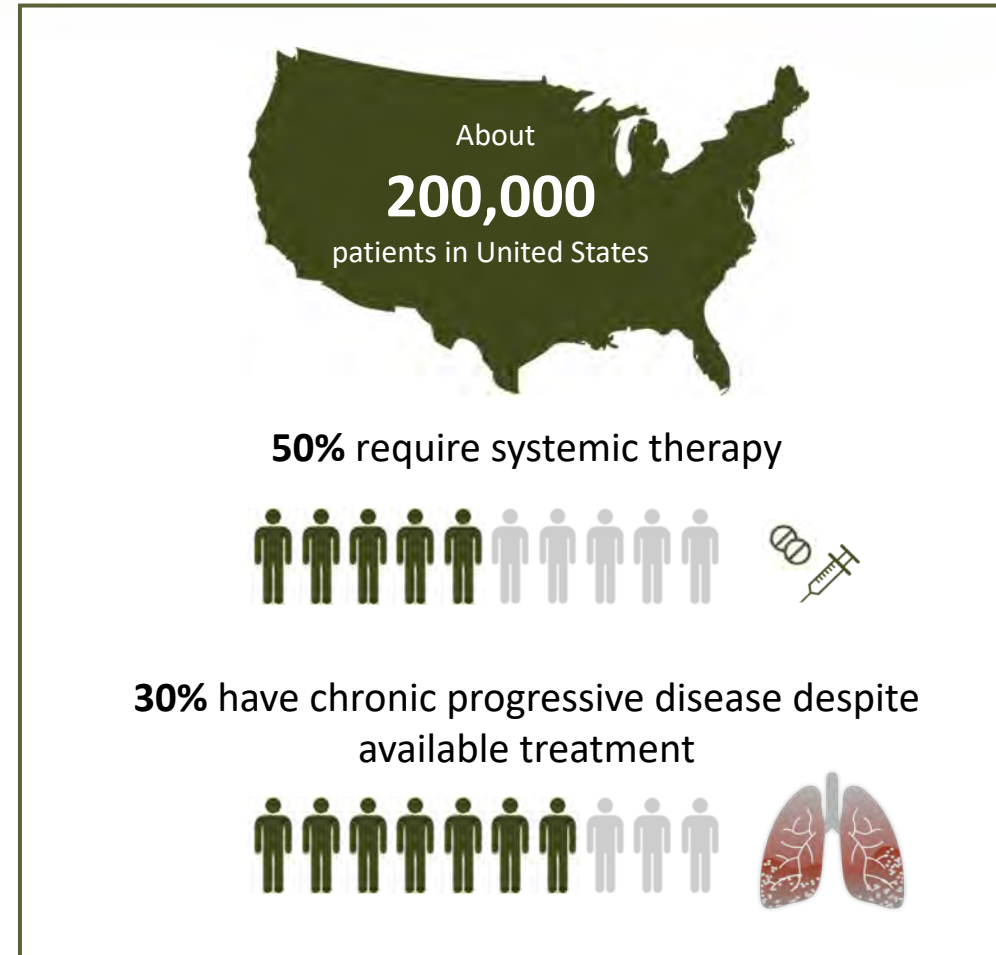
(1) Lederer, Martinez. NEJM 2018

(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

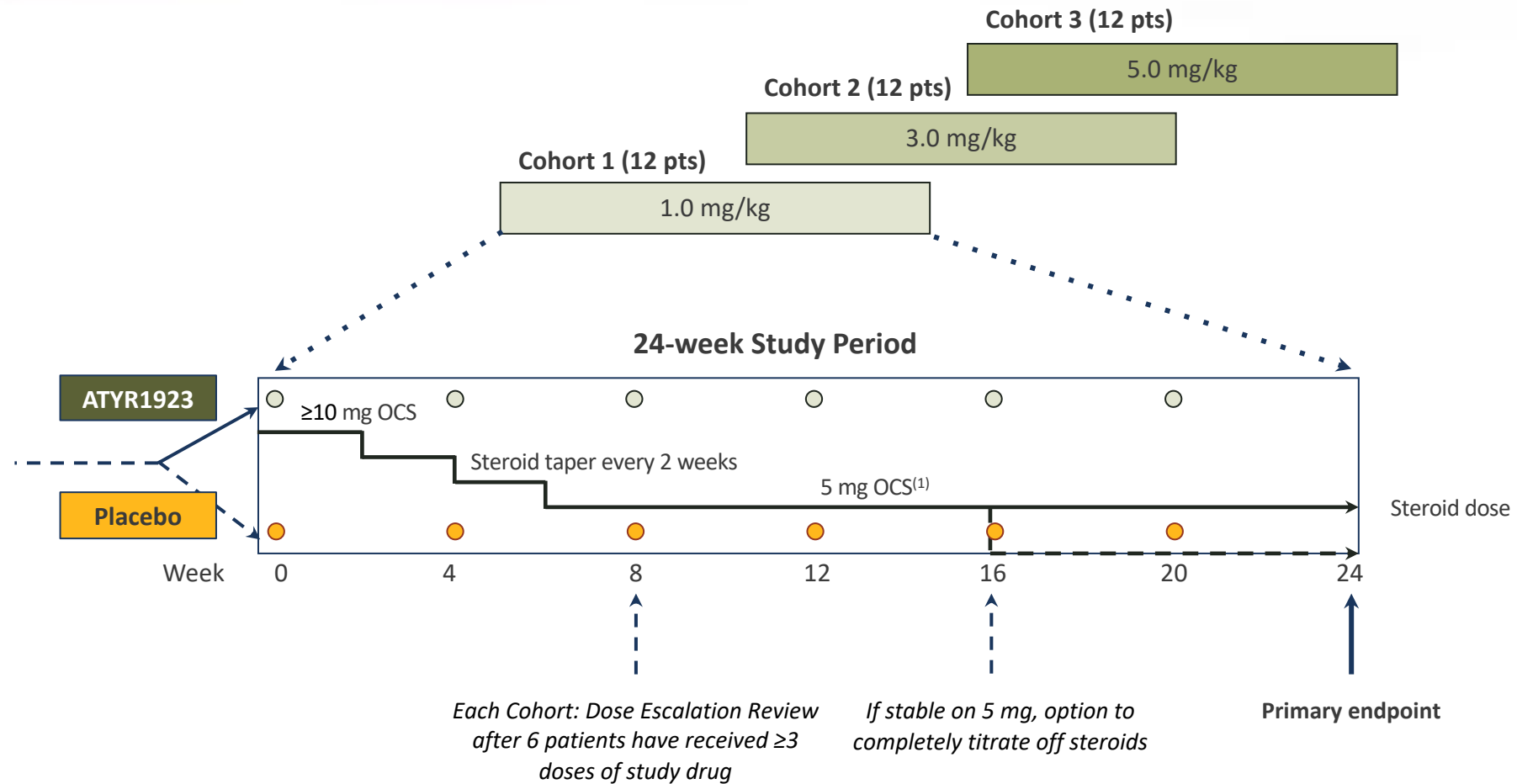


Phase 1b/2a Study in Pulmonary Sarcoidosis Ongoing

Design	<ul style="list-style-type: none">• Randomized (2:1), double-blind, placebo-controlled, multiple ascending dose• 6 IV doses of ATYR1923 being tested at 1.0, 3.0, and 5.0 mg/kg• Forced steroid taper to 5.0 mg by week 8; taper to 0 mg possible at week 16 in responders
Population	<ul style="list-style-type: none">• 36 histologically confirmed pulmonary sarcoidosis patients• ≥10 mg stable oral corticosteroid treatment• Symptomatic/active disease at baseline
Primary Endpoint	<ul style="list-style-type: none">• Safety and tolerability of multiple ascending IV ATYR1923 doses
Secondary Endpoints	<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

Target enrollment completed
Data expected Q3 2021

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: \$1.2b 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

Last subject visit completed for Phase 1 study to evaluate the safety, pharmacokinetics and immunogenicity in Japanese healthy volunteers

ATYR1923

COVID-19 Related Severe Respiratory Complications

Phase 2 Study in COVID-19 Related Severe Respiratory Complications

Rationale	<ul style="list-style-type: none">• COVID-19 associated lung inflammation is driven by pathways effected by ATYR1923's mechanism of action
Objective	<ul style="list-style-type: none">• Evaluate safety and preliminary efficacy of ATYR1923 in subjects hospitalized with COVID-19-related severe respiratory complications
Design	<ul style="list-style-type: none">• Randomized, double-blind, placebo controlled, single dose (not powered for statistical significance)
Population	<ul style="list-style-type: none">• 32 adult patients with severe respiratory complications related to COVID-19 infection requiring supplemental oxygen but not mechanically ventilated (WHO score 4, 5)
Doses	<ul style="list-style-type: none">• Randomized 1:1:1 - Single dose of 1.0 or 3.0 mg/kg ATYR1923 or Placebo
Endpoints	<ul style="list-style-type: none">• Primary: Safety and Tolerability• Secondary: Time to recovery (WHO score ≤ 3 or hospital discharge without supplemental oxygen); proportion of patients achieving recovery within a week; all cause mortality• Exploratory: Clinical biomarkers; 60 day follow up

Topline data reported January 2021

Full data set, including biomarker analysis, expected Q1 2021

Highlights of Topline Results for Safety and Key Recovery Metrics

Study Met Primary Safety Endpoint in Moderate to Severe Hospitalized Patients

- ATYR1923 was generally safe and well-tolerated in both the 1.0 and 3.0 mg/kg treatment groups
- Adverse events were mostly mild or moderate in severity and there were no drug-related SAEs

Preliminary Signal of Activity Seen in 3.0 mg/kg Cohort⁽¹⁾

- 3.0 mg/kg cohort experienced a median time to recovery of 5.5 days (95% CI: 3,6) compared to 6 days (95% CI: 2,12) in placebo group
- 83% vs 56% of patients achieved recovery by day 6 in the 3.0 mg/kg ATYR1923 and placebo groups, respectively

Key Insights from Preliminary Demographics and Baseline Characteristics

- Demographics and baseline disease characteristics were largely balanced except for some key risk factors which were disproportionately randomized to ATYR1923 groups:
 - More patients over the age of 65
 - More patients with severe hypoxia
 - More baseline comorbidities and more patients with multiple baseline comorbidities
- Imbalances suggest a sicker patient population in ATYR1923 treatment groups and may have contributed to an overperformance in the placebo arm
- All patients in the study received remdesivir and/or dexamethasone



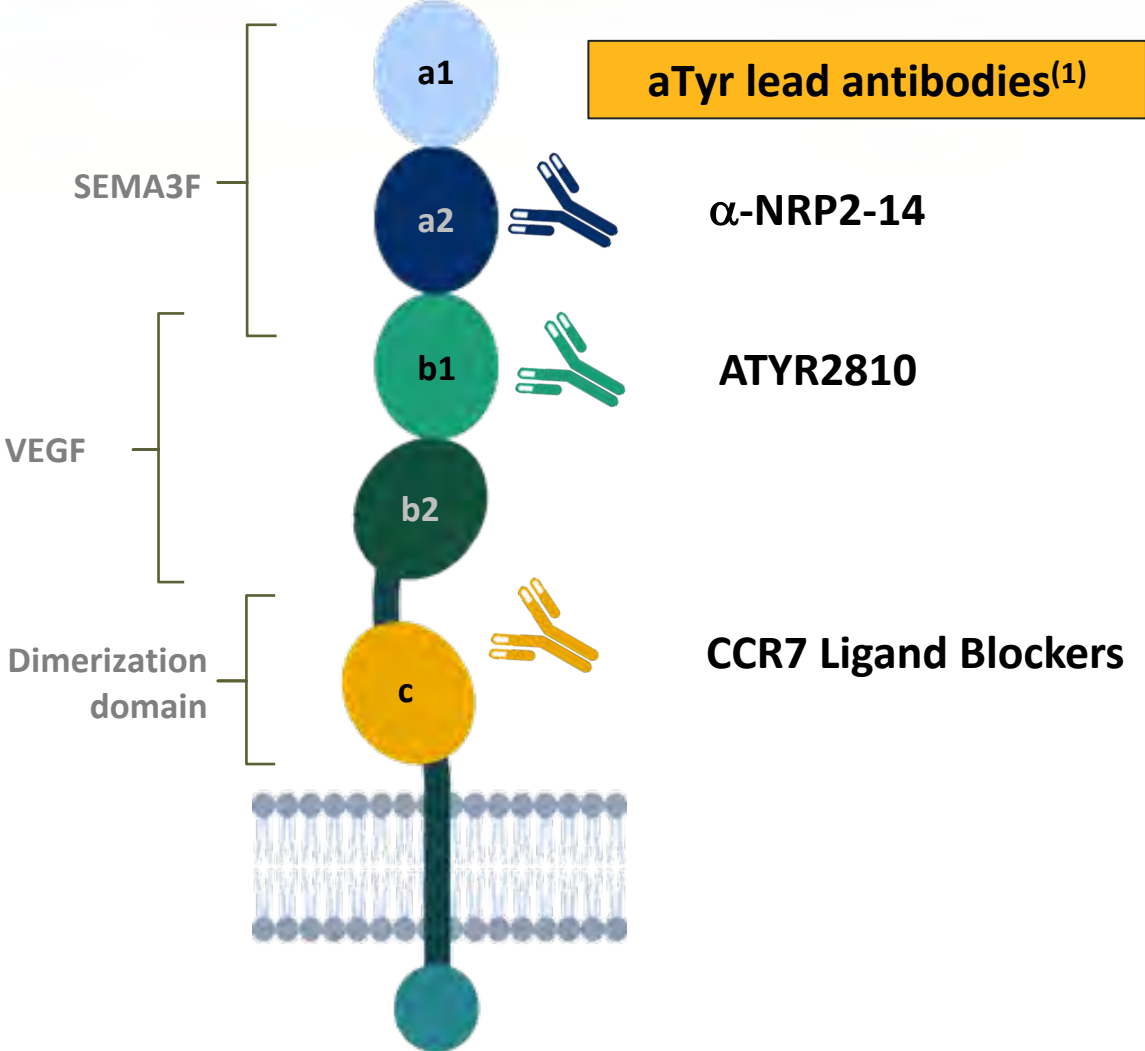
NRP2 Antibodies

Regulating Diverse Disease Pathways

NRP2: A Novel Therapeutic Target

- NRP2 is a potentially novel drug target for cancer and inflammatory disorders
- Acts as a co-receptor for VEGF, semaphorins and certain chemokines (e.g., CCL19)
- Highly expressed on certain tumors and upregulated on immune cells during inflammation
- Highly expressed on key immune cells in the tumor microenvironment that are implicated in cancer progression, including MDSCs, DCs, Tregs and TAMs generated from triple negative breast cancer cell lines⁽¹⁾
- Tumor expression is associated with worse outcomes in many cancers
- aTyr has developed a panel of antibodies to selectively target different NRP2 epitopes for diverse therapeutic applications
- aTyr anti-NRP2 monoclonal antibodies exhibit superior specificity and sensitivity compared to commercially available antibodies

aTyr is Developing Humanized NRP2 Antibodies Targeting Diverse Pathways



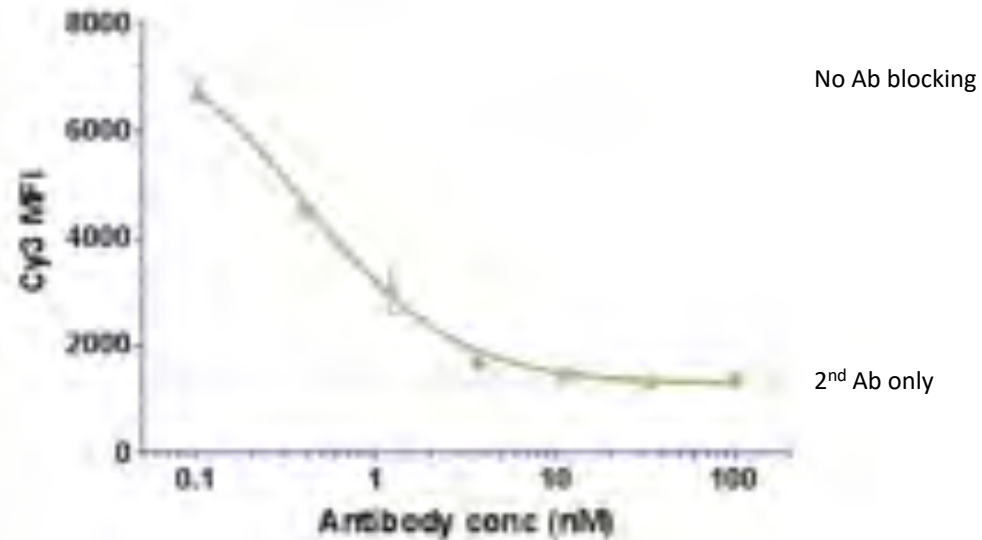
(1) Distinct from ATYR1923 interaction with NRP2

ATYR2810: Lead Anti-Neuropilin-2 Antibody IND Candidate for Cancer

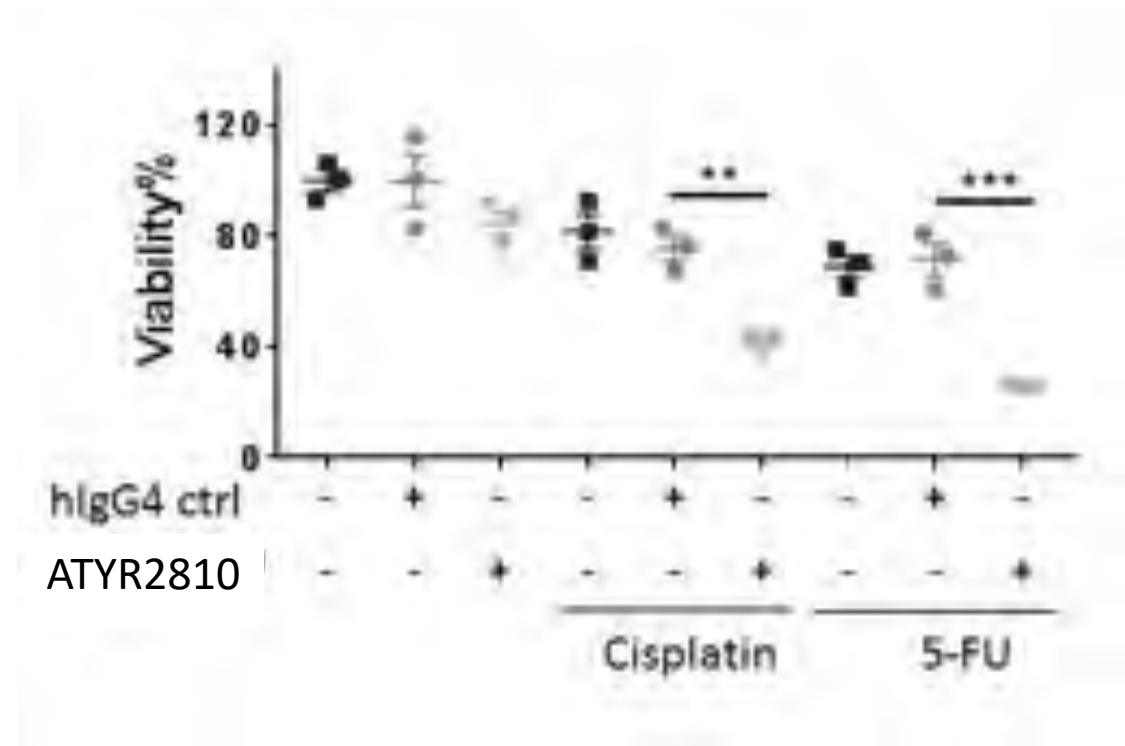
- ATYR2810 is a humanized monoclonal antibody that specifically and functionally blocks the interaction between NRP2 and VEGF
- The role of NRP2 and VEGF signaling in the tumor microenvironment and its importance in the progression of certain aggressive cancers is becoming increasingly validated
- Preclinical data in models of triple-negative breast cancer suggest that ATYR2810 could potentially be effective in certain aggressive solid tumors ⁽¹⁾
 - Blocks VEGF-C binding to NRP2
 - Shows tumor inhibitory effects
 - Increases sensitivity to chemotherapy

Early Pre-clinical Data Support Development in Oncology

Blocks VEGF binding to NRP2



Increases Sensitivity to Chemotherapy in Triple-Negative Breast Cancer Model





aTyr

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
- Novel approach for identifying target receptors for extracellular tRNA synthetase fragments
- 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
- Lead program ATYR1923 is based on a naturally occurring splice variant of one of these families, histidyl-tRNA synthetase (HARS)
- Recent discovery of new receptor targets for two tRNA synthetases—alanyl-tRNA Synthetase (AARS) and aspartyl-tRNA Synthetase (DARS)— in cancer and inflammation.
- Discovery programs initiated for AARS and DARS primarily targeting cancer and initially focusing on natural killer (NK) cell biology.

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aTyr

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 1b/2a clinical study in pulmonary sarcoidosis completed enrollment in US – positive interim safety data reported Dec 2019
 - Kyorin collaboration for ILD in Japan with total deal value up to \$175m – completed last subject visit for Phase 1 study
 - Phase 2 trial in COVID-19 patients with severe respiratory complications completed – positive topline results reported January 2021
- Preclinical program: ATYR2810
 - Lead anti-NRP2 antibody IND candidate for cancer shows anti-tumor effects in triple-negative breast cancer model
- Discovery stage programs in cancer, inflammation and immunology
 - NRP2 antibody research program for distinct therapeutic applications
 - Discovery programs for tRNA synthetases AARS and DARS primarily targeting cancer and initially focusing on NK cell biology
- Cash, cash equivalents, and investments at \$36.1m as of September 30, 2020

Upcoming Catalysts

ATYR1923

- Phase 1b/2a results in pulmonary sarcoidosis patients expected Q3 2021
 - Kyorin's Phase 1 in healthy volunteers to support trials for ILD in Japan completed last subject visit in January 2021
 - Phase 2 full data set in COVID-19 patients expected Q1 2021
-

ATYR2810

- IND enabling activities for the first anti-NRP2 antibody
-

NRP2 Antibodies

- Potential new pipeline opportunities internally and through academic collaborations
-

tRNA Synthetase Candidates

- Presentation of scientific findings related to new receptor targets for AARS and DARS
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Thank You