A New Path to Medicine

Oppenheimer 31st Annual Healthcare Conference

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March 16-17, 2021

Forward Looking Statements

The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” “opportunity,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements regarding: the potential therapeutic benefits of proteins derived from tRNA synthetase genes and our product candidates, including ATYR1923 and ATYR2810, and development programs, including our NRP2 antibody program and our tRNA synthetase program; the ability to successfully advance our product candidates and undertake certain development activities (such as the initiation of clinical trials, clinical trials enrollment, the conduct of clinical trials and announcement of clinical results) and accomplish certain development goals, and the timing of such events; the potential market opportunity for our product candidates; our ability to receive regulatory approvals for, and commercialize, our product candidates; our ability to identify and discover additional product candidates; potential activities and payments under collaboration agreements; and the ability of our intellectual property portfolio to provide protection are forward-looking statements. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These risks, uncertainties and other factors are more fully described in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, and in our other filings. The forward-looking statements in this presentation speak only as of the date of this presentation and neither we nor any other person assume responsibility for the accuracy and completeness of any forward-looking statement. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

aTyr: A New Path to Medicine

Mission: Develop a new class of medicines based on proprietary biology platform with a novel approach for identifying target receptors for extracellular tRNA synthetase fragments from an IP portfolio covering protein derivatives from all 20 tRNA synthetase gene families

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

tRNA Synthetase Candidates

- Receptors identified for two new tRNA synthetases from our pipeline
- Discovery programs targeting cancer and NK cell biology

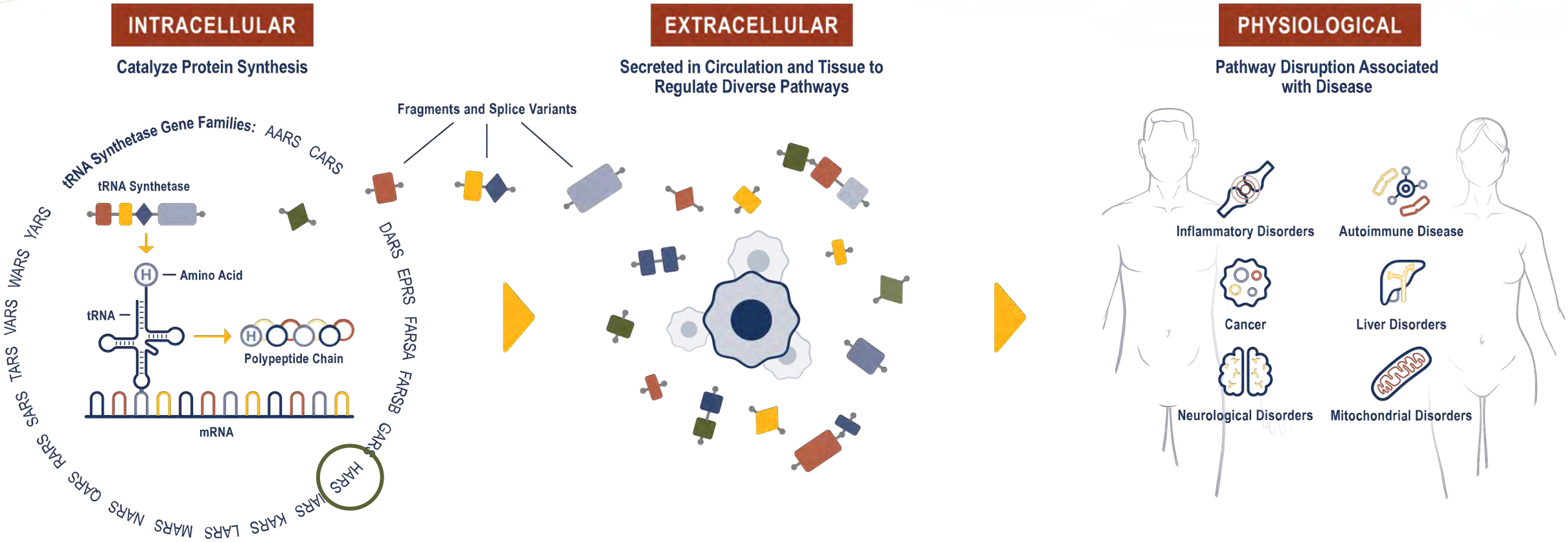
Financials: Cash, cash equivalents and investments at $36.1m as of September 30, 2020

aTyr Development Pipeline

PROGRAM	INDICATION	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
ATYR1923	Pulmonary Sarcoidosis					
	Other ILDs (CTD-ILD; CHP)(1)					
	Healthy Japanese Volunteers(2)					
	COVID-19 related severe respiratory complications					
ATYR2810	Solid Tumors					
NRP2 mAbs	Cancer; Inflammation					
tRNA Synthetase Candidates	Cancer; Fibrosis; Inflammation					

(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.

tRNA Synthetases May Have Novel Functions Extracellularly



tRNA synthetases are secreted extracellularly and occur in novel forms which lose their canonical function

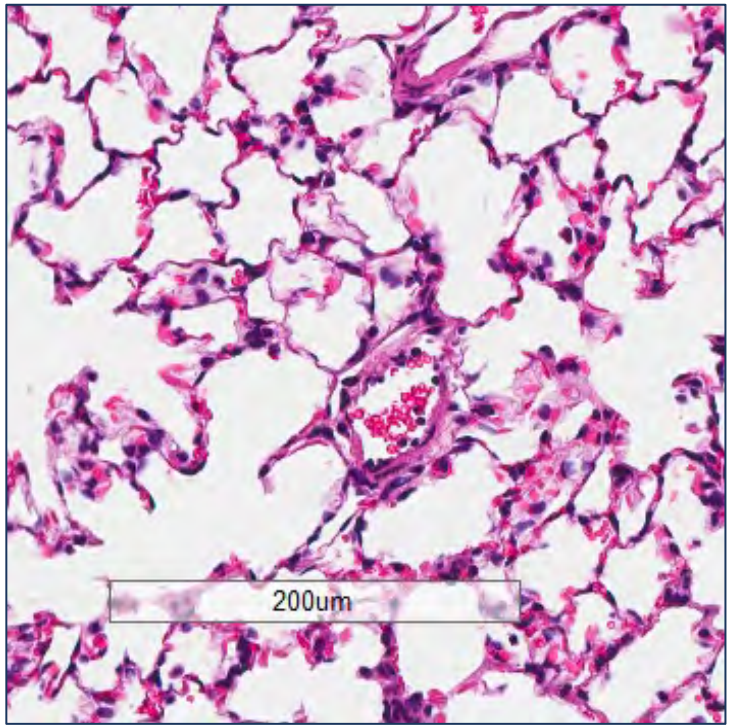
Extracellular tRNA synthetase disruption (genetic/ autoimmune) is associated with disease in humans

ATYR1923

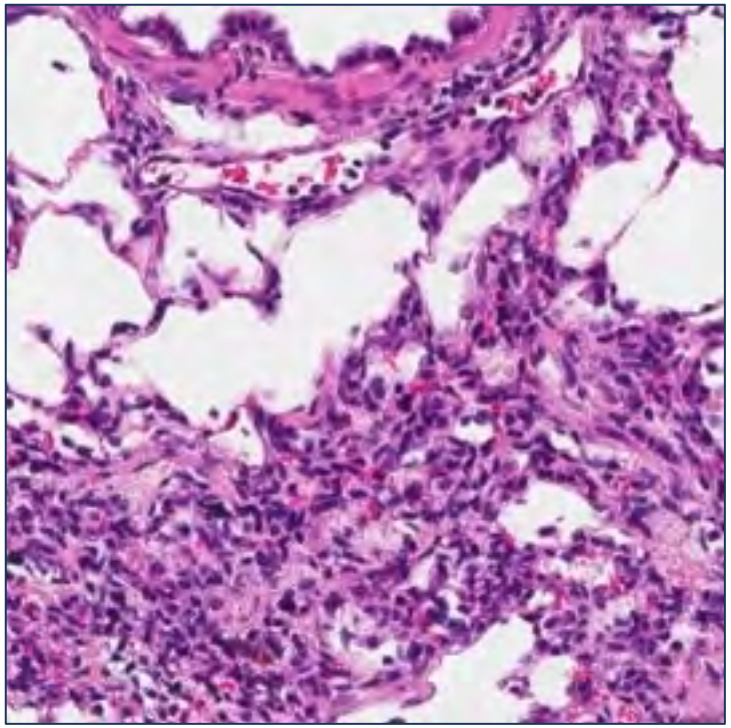
A Novel Immunomodulator for Inflammatory Lung Disease

A Novel Mechanism to Treat Inflammation

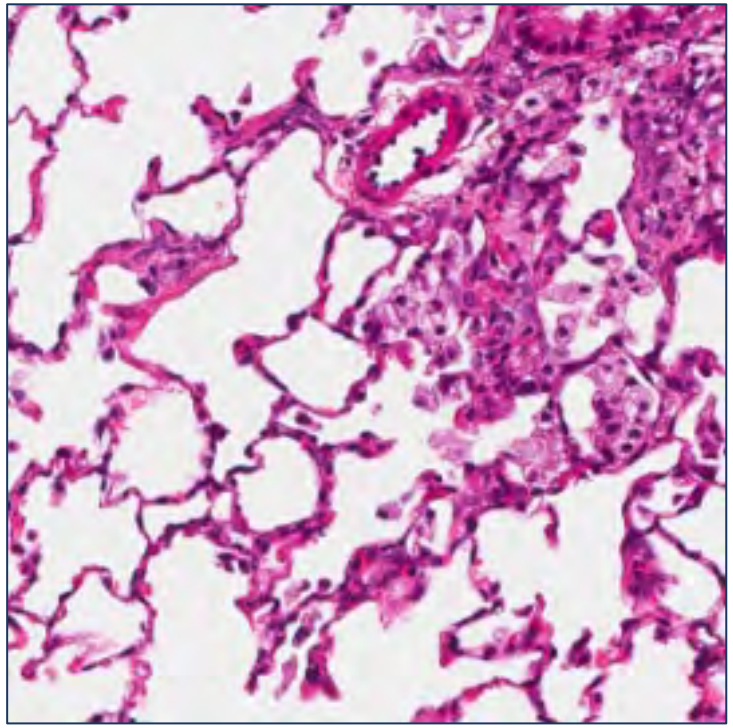
Healthy lung



Injured lung



ATYR1923 treated



Representative histology showing immune cell infiltrate in a rat model of bleomycin induced lung fibrosis presented at the American Thoracic Society annual meeting 2018.

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

- Fc fusion protein, based on naturally occurring splice variant of the 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

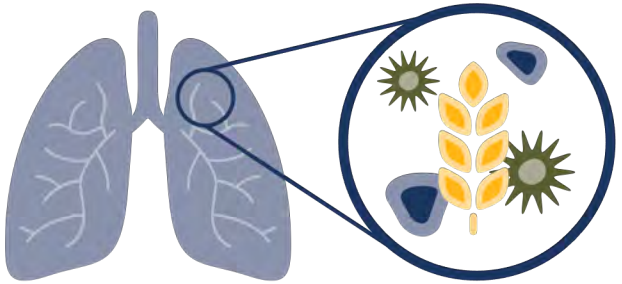
P. acnes (Sarcoidosis)	↓ pro-fibrotic proteins
S. Rectivirgula (CHP)	↓ tissue cytokines/chemokines and enzymes
Sclerodermatous GvHD (SSc-ILD)	↓ fibrosis
SKG mice (RA-ILD)	↓ immune infiltrates
Bleomycin-Induced Lung Fibrosis (IPF)	↓ inflammation / fibrosis

Consistent downregulation of pro-inflammatory cytokines including IL-6, MCP-1, and IFN-γ

Data available at https://www.atyrpharma.com/our-science/publications/

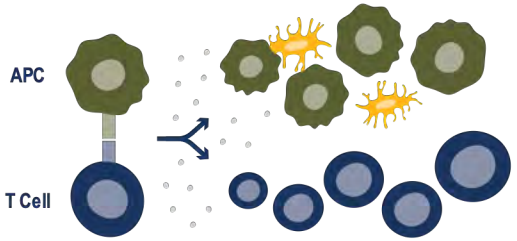
ATYR1923 Mechanism of Action in Inflammatory Lung Disease

Disease Trigger



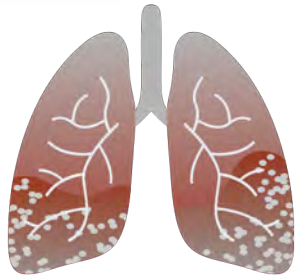
Organic; inorganic; infectious; autoimmune

Aberrant Immune Responses



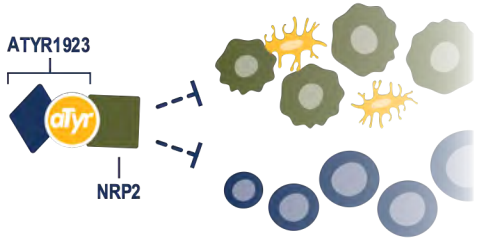
T-cell activation; Pro-inflammatory cytokine/chemokines triggering fibrotic pathways; NRP2 upregulation on immune cells

Lung Inflammation & Fibrosis



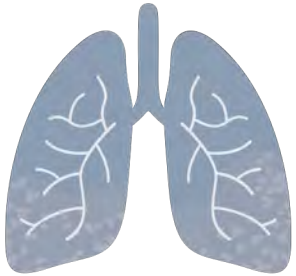
Persistent, unresolved inflammation in the lung can lead to fibrosis; patients experience chronic cough, dyspnea, mortality

ATYR1923 Dampens Immune Responses



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

Stabilized Lung



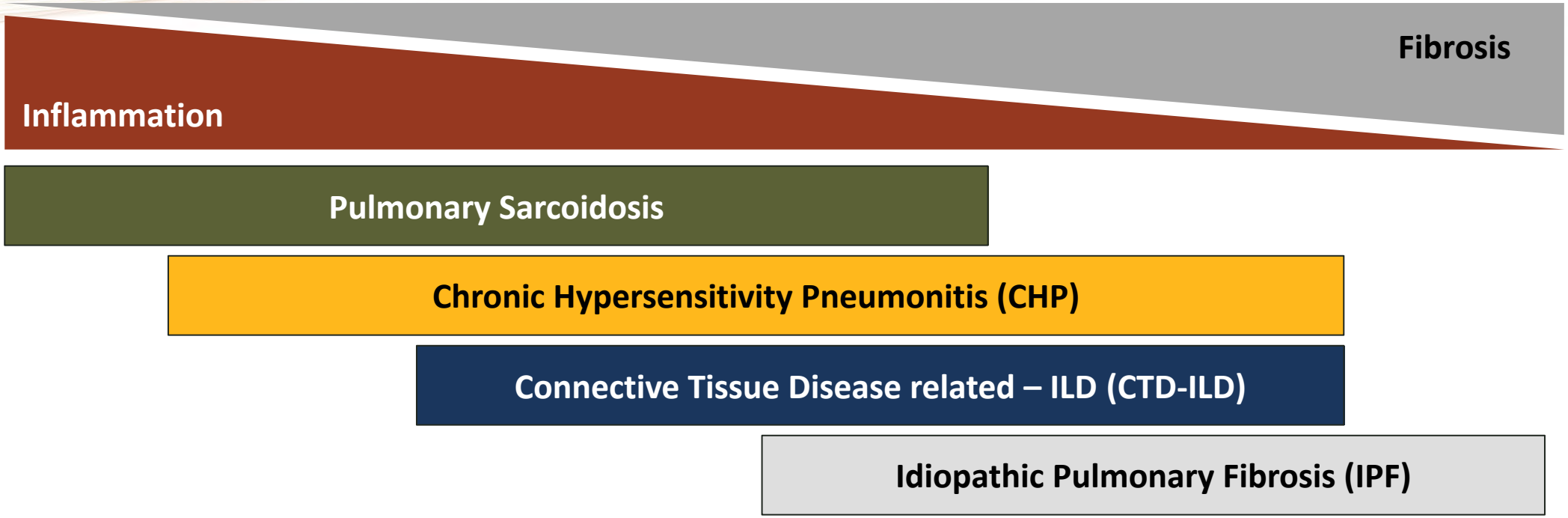
Reduced inflammation and fibrotic deposition; symptom relief, stabilized lung function*

*aTyr hypothesis

ATYR1923

Interstitial Lung Disease

ILDs Share Common Immune Pathology Leading to Fibrosis

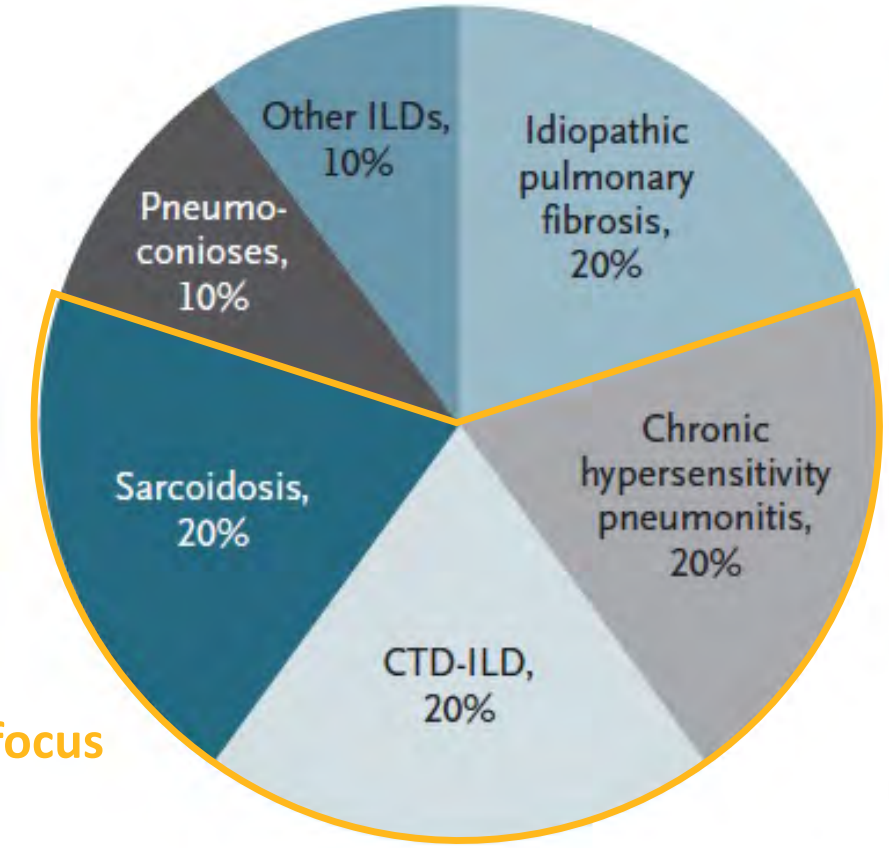


- ILDs lie on a spectrum of inflammation and fibrosis, but all share an immune pathology
- Progression to fibrosis is a key driver of morbidity and mortality
- By targeting aberrant immune response driving fibrosis, ATYR1923 has potential to improve outcomes in multiple ILDs

Slide adapted from Dr. Steven Nathan, Medical Director, Advanced Lung Disease and Transplant Program at Inova Fairfax Hospital, Falls Church, VA

Market Opportunity in Inflammatory Interstitial Lung Disease

Relative Distribution of ILDs in the USA(1)



- >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

50% require systemic therapy

30% have chronic progressive disease despite available treatment

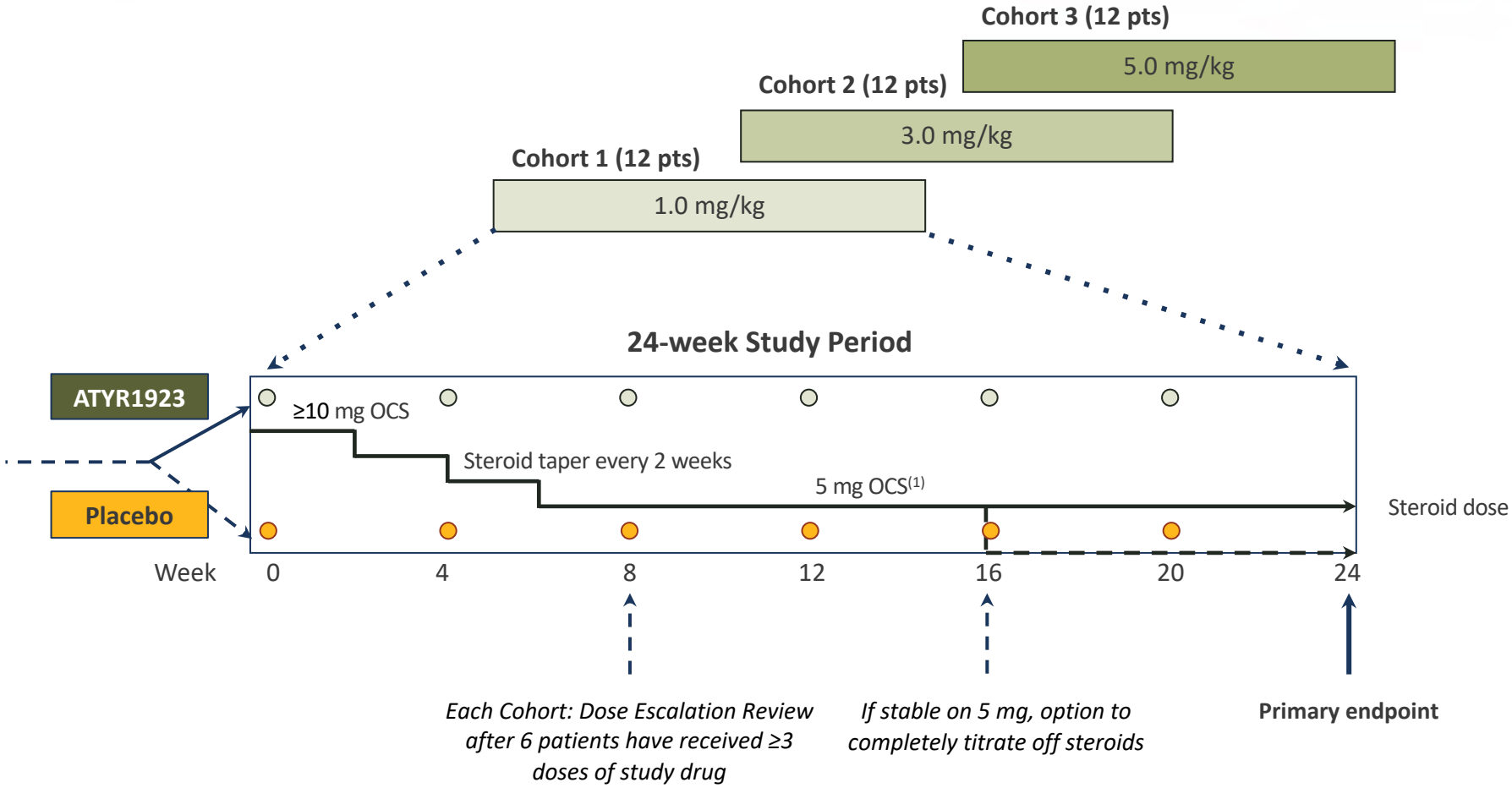
Culver et al. BMJ 2019; Baughman ATS Annals 2016

Phase 1b/2a Study in Pulmonary Sarcoidosis Ongoing

Design	• 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	• 37 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

Target enrollment completed
Data expected Q3 2021

Phase 1b/2a Pulmonary Sarcoidosis Study Schema



(1) subtherapeutic dose

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 and milestone payments: $10m
- Development, regulatory and commercial milestones: $165m
- 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	• COVID-19 associated lung inflammation is driven by pathways effected by ATYR1923's mechanism of action
Objective	• Evaluate safety and preliminary efficacy of ATYR1923 in subjects hospitalized with COVID-19-related severe respiratory complications
Design	• Randomized, double-blind, placebo controlled, single dose (not powered for statistical significance)
Population	• 32 adult patients with severe respiratory complications related to COVID-19 infection requiring supplemental oxygen but not mechanically ventilated (WHO score 4, 5)
Doses	• Randomized 1:1:1 - Single dose of 1.0 or 3.0 mg/kg ATYR1923 or Placebo
Endpoints	• 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

(1) Study was not powered for statistical significance

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

Biomarker Data Demonstrates Anti-Inflammatory Effects

- Patients treated with ATYR1923 demonstrated trends of overall improvement in key biomarkers analyzed compared to placebo
  - Greater reductions in levels of several key inflammatory cytokines and chemokines including interferon gamma (IFNγ), interleukin-6 (IL-6) and monocyte chemoattractant protein 1(MCP-1)
  - Statistically significant reduction in levels of serum amyloid A (SAA), a marker of inflammation and fibrosis that has implications in sarcoidosis and other ILDs
- The cytokines reduced to the greatest extent as a result of ATYR1923 treatment are consistent with animal models
- Biomarker data confirms that at baseline, patients enrolled in the ATYR1923 treatment arms compared to placebo had higher levels of inflammatory cytokines and known COVID-19 biomarkers including ferritin, D-dimer and C-reactive protein (CRP), indicating a more inflamed patient population in the ATYR1923 treatment arms

NRP2 Antibodies

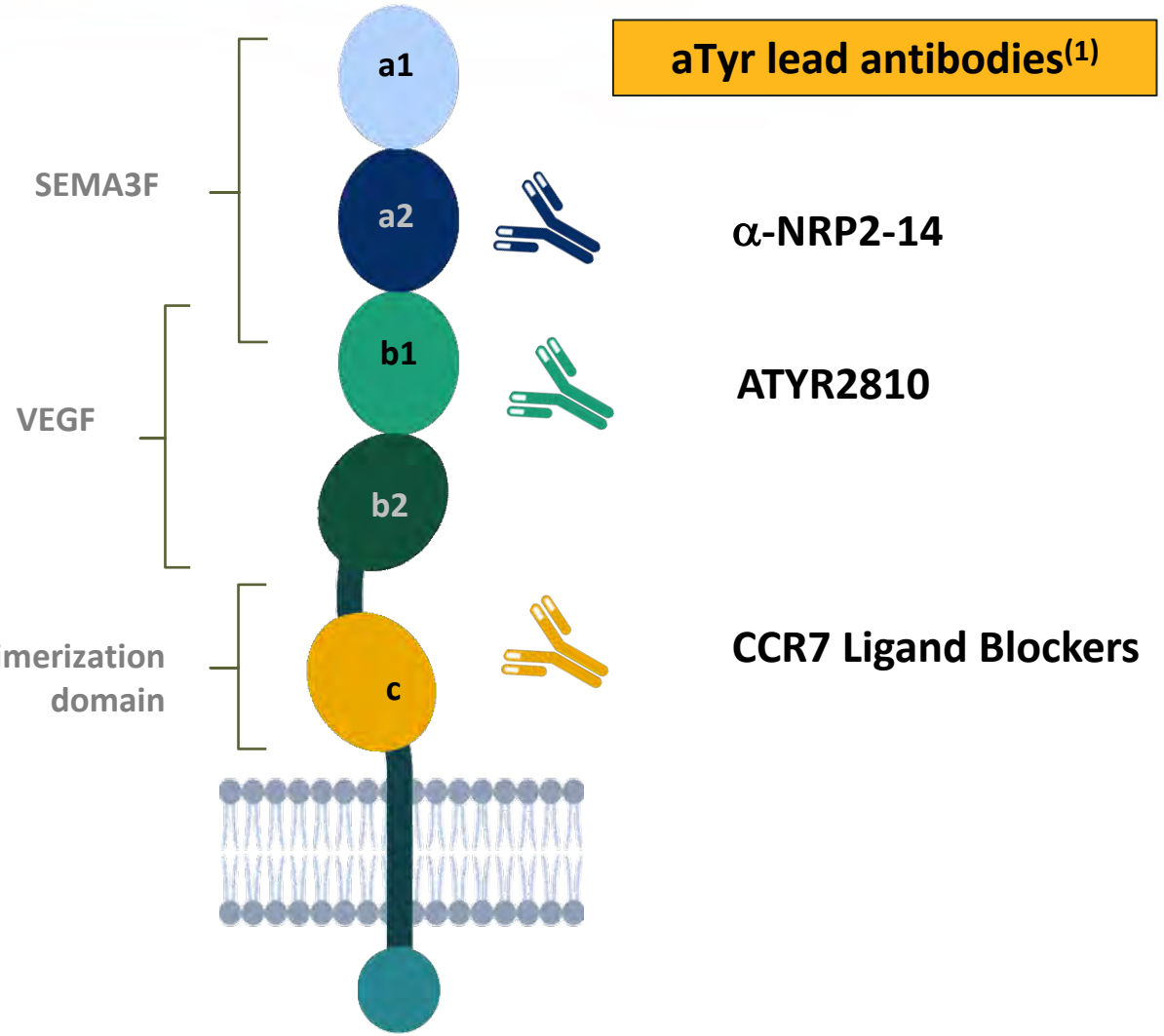
Regulating Diverse Disease Pathways

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., CCL21)
- Highly expressed on certain solid tumors, such as breast and lung
- Tumor expression is associated with worse outcomes in many cancers

aTyr is Developing Humanized NRP2 Antibodies Targeting Diverse Pathways

- 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



(1) Distinct from ATYR1923 interaction with NRP2

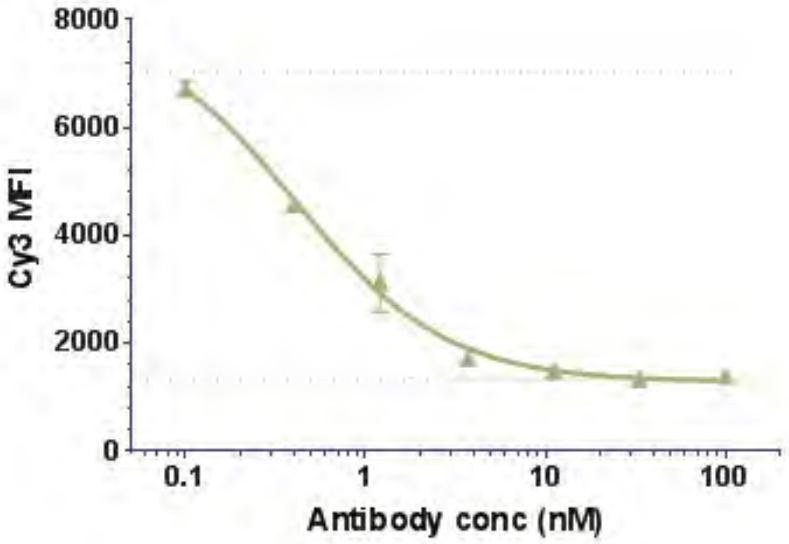
ATYR2810: Lead Anti-Neuropilin-2 Antibody IND Candidate for Cancer

- 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

(1) Domain-Specific Antibodies to Neuropilin 2 Implicate VEGF-C and not Semaforin 3F in Breast Cancer Stem Cell Function. American Association for Cancer Research, 2020

Early Pre-clinical Data Support Development in Oncology

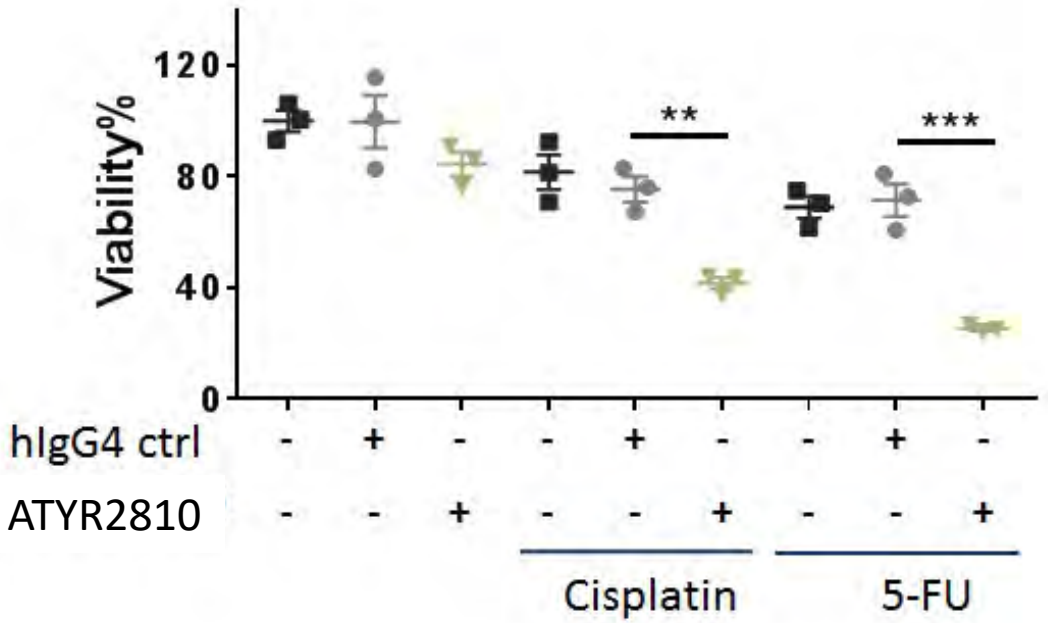
Blocks VEGF binding to NRP2



No Ab blocking

2nd Ab only

Increases Sensitivity to Chemotherapy in Triple-Negative Breast Cancer Model



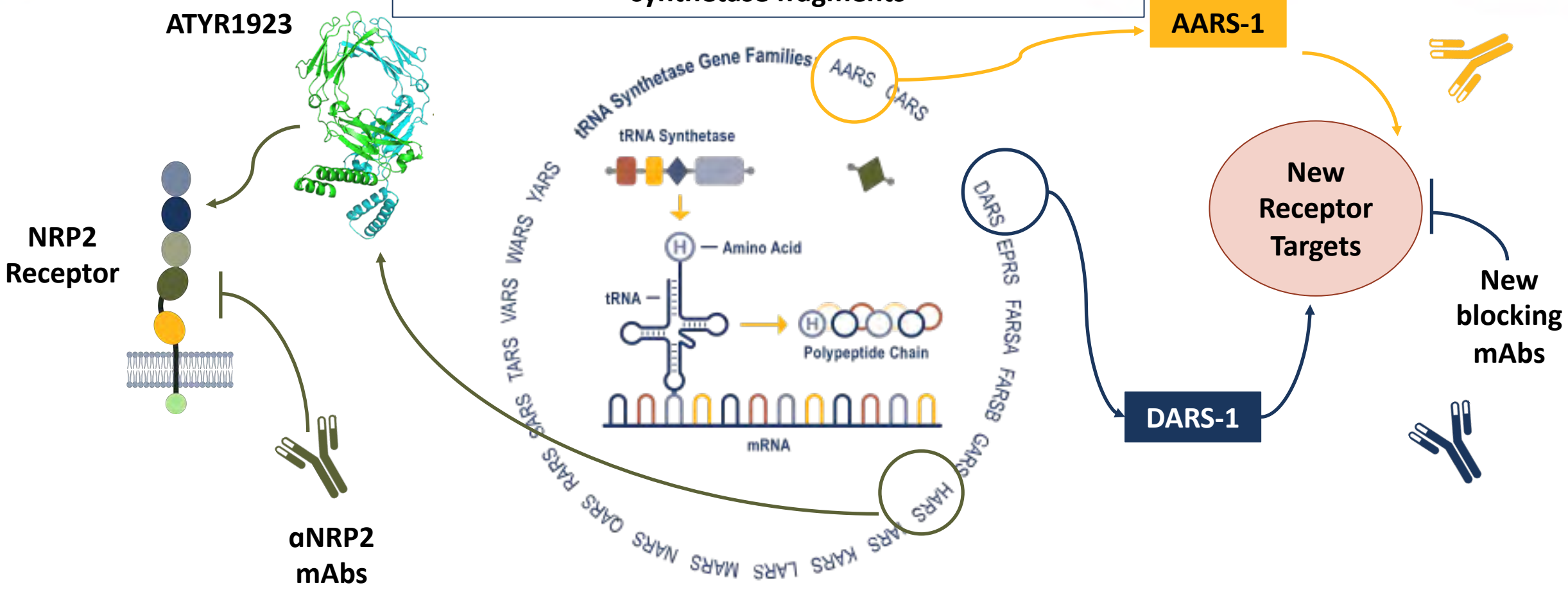
AACR Virtual Meeting II – June 22-24, 2020; *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0..0001

tRNA Synthetases

A Potential New Therapeutic Protein Class

aTyr Biology Platform

Novel approach for identifying target receptors for tRNA synthetase fragments

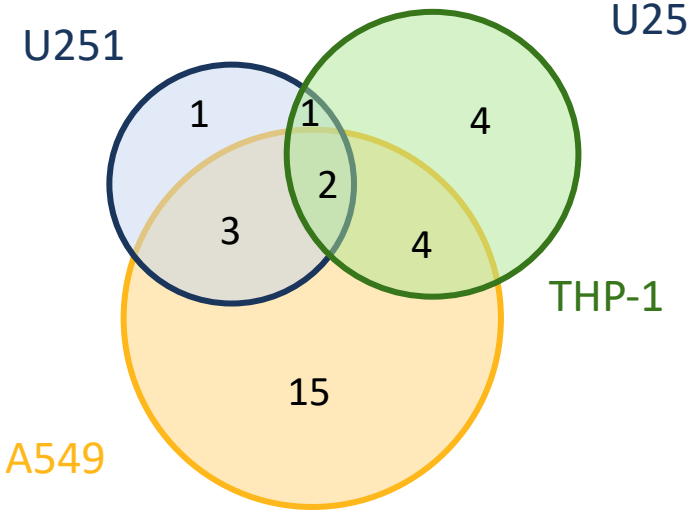


aTyr owns IP covering all 20 tRNA synthetase gene families

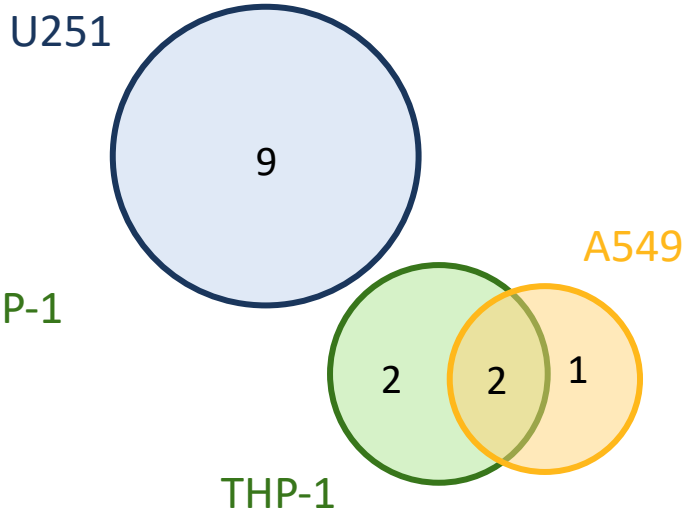
New Discovery Programs Initiated from tRNA Synthetase Library

- New discovery programs initiated around select fragments of alanine- (AARS) and aspartyl- (DARS) tRNA synthetases from our platform library
- Multiple binding targets identified using novel approach, with potential implications in immunology, fibrosis and cancer
- Initial focus on NK cells for cancer

AARS-1 Receptor ID



DARS-1 Receptor ID



Differential Cell Binding

	Human cell type	Differentiation state	AARS-1	DARS-1
Innate Immune cells	Monocyte THP-1	Naïve	+	+
	Primary monocytes (classical)	Naïve	-	-
	Primary monocytes (classical)	Activated (PMA)	++	++
	Monocyte THP-1	M0 (PMA)	+	+
	Monocyte THP-1	M1 (PMA/LPS/IFNγ)	-	-
	Primary macrophages	All	-	+
	Natural Killer NK-92	Naïve	-	++
	Primary NK cells	Naïve	+	+
Adaptive Immune cells	T cell Jurkat	Naïve	+	+
	T cell Jurkat	Activated (αCD3/αCD28)	+	+
	T cell Jurkat	Activated (PMA)	-	-
	Primary CD4+ T-cells	CD4+	-	-
	Primary CD8+ T-cells	CD8+	+	+
	Primary NK-T cells	Naïve	+	+
Oncology	Glioblastoma U251	Naïve	++	++
	Glioblastoma U87	Naïve	+	+
	Lung adenocarcinoma A549	Naïve	++	++

Presented at SLAS 2021

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 and positive biomarker data reported March 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 • 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

Thank You