aTyr Pharma
NASDAQ: LIFE

Translating New Immune Pathways into Meaningful Medicines

Baird 2018 Global Healthcare Conference

Sanjay S. Shukla, M.D., M.S., President & CEO

September 6, 2018

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 we make regarding the potential therapeutic benefits of proteins derived from tRNA synthetase genes and our product candidates, including ATYR1923 and any product candidates from our other pipeline programs, the ability to successfully advance our pipeline or product candidates, the timing within which we expect to initiate, receive and report data from, and complete our planned clinical trials, our ability to receive regulatory approvals for, and commercialize, our product candidates, our ability to identify and discover additional product candidates, 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.

Corporate Overview - aTyr

Founded: 2005 by Paul Schimmel, Ph.D. and Xiang-Lei Yang, Ph.D, leading tRNA synthetase researchers at *The Scripps Research Institute (TSRI)*

Science: Discovering and developing novel therapeutics based on our understanding of the extracellular functionalities of tRNA synthetase genes

Publication: *Human tRNA Synthetase Catalytic Nulls with Diverse Functions.* Science 2014.

Patents: Global intellectual property estate directed to a potential pipeline of protein compositions derived from 20 tRNA synthetase genes

Located: San Diego, CA

Subsidiary: Pangu BioPharma (98%), founded in Hong Kong, affiliated with tRNA synthetase research at *Hong Kong University of Science & Technology (HKUST)*

Accelerating Value Creation from Novel Biology

Platform of New Biology:

Discover innovative therapeutic candidates based on proprietary knowledge of extracellular functions of tRNA synthetase genes

Lead Product Candidate: ATYR1923

Engineered protein, based on the HARS* gene, for the treatment of interstitial lung diseases

Financials:

Cash, cash equivalents and investments at $64.3M as of 6/30/2018

Upcoming Clinical Catalysts:

- ✓ ATYR1923 Phase 1 data – 2Q 2018
- ❑ Initiate Phase 1b/2a – 4Q 2018
- ❑ Results Phase 1b/2a – TBD†

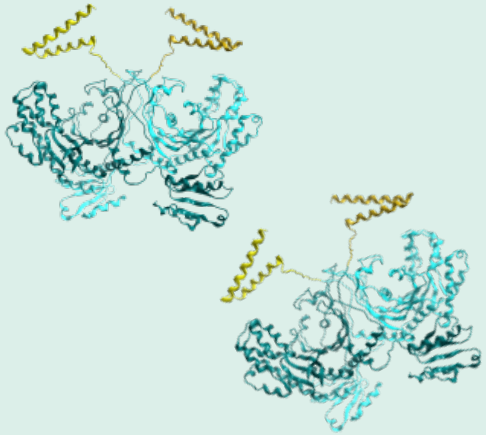
†Based on indication selection/protocol

aTyr Pharma NASDAQ: LIFE

HARS **–** the histidyl-tRNA synthetase (HARS) gene, one of 20 tRNA synthetase genes

New Biology: Functionality of Extracellular tRNA Synthetase Proteins

tRNA Synthetase Genes



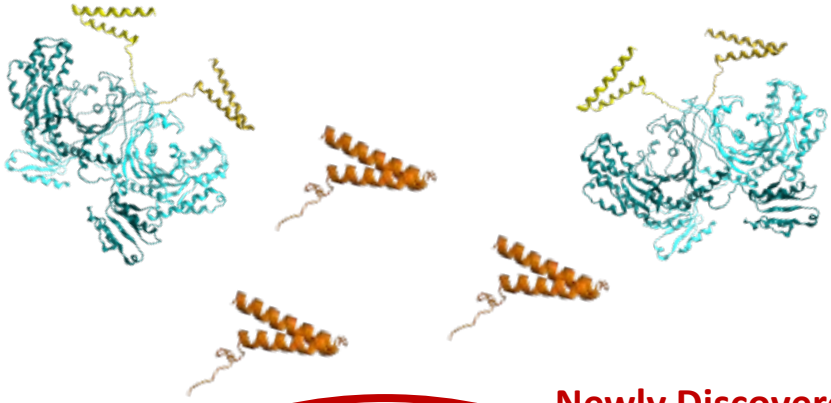
Intracellular function:
Supports protein synthesis, connects amino acid to tRNA

Cytoplasm

Secretion

Cell membrane

Extracellular Proteins
(full-length and splice-variants)
derived from tRNA synthetase genes

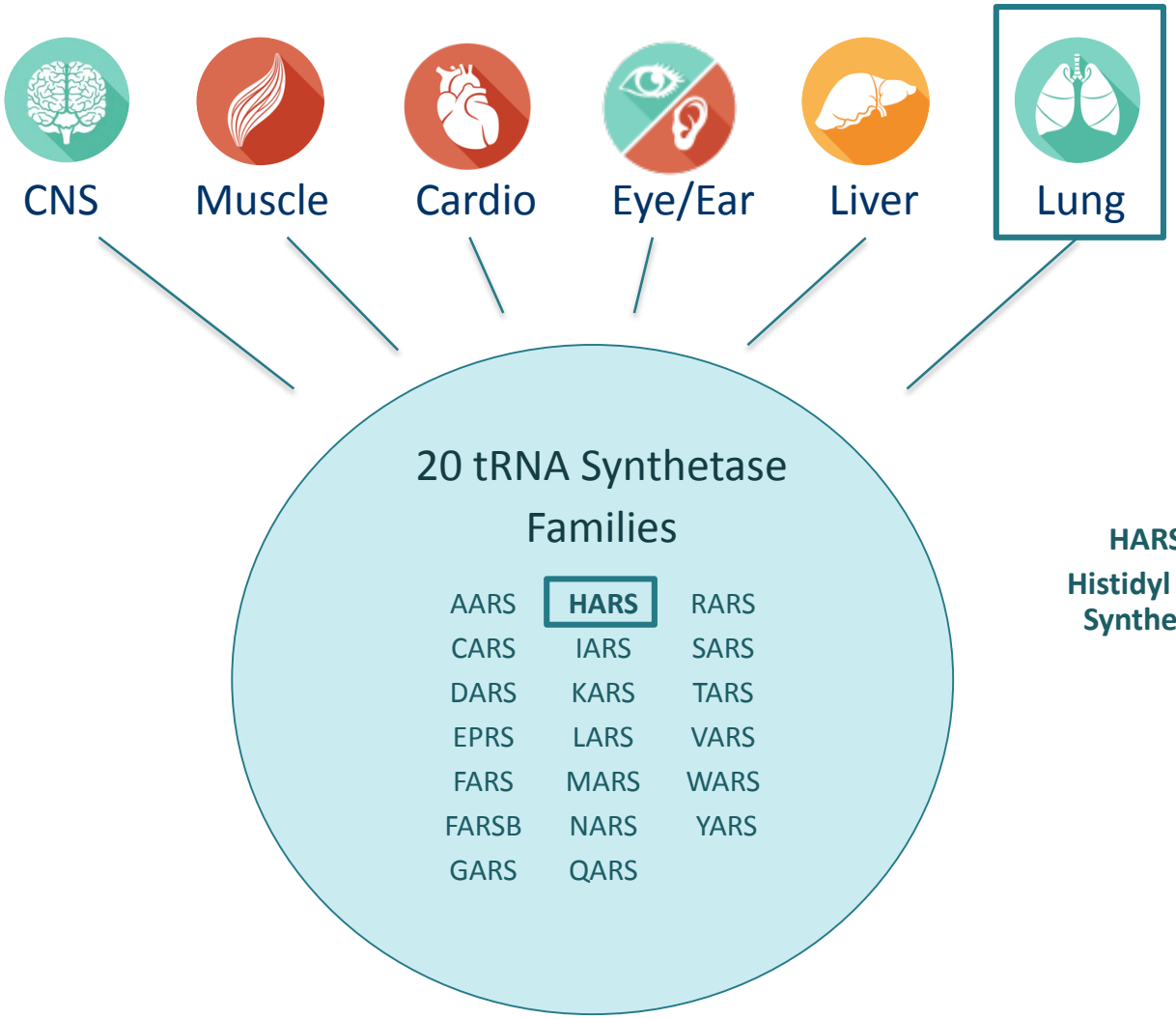


Newly Discovered Biology

Extracellular function:
Additional & discrete functions in circulation

Circulation

Extracellular tRNA Synthetase Biology Associated with Disease



HARS = Histidyl tRNA Synthetase

ATYR1923: Program Snapshot

ATYR1923:

Extracellular HARS splice variant "iMod domain"

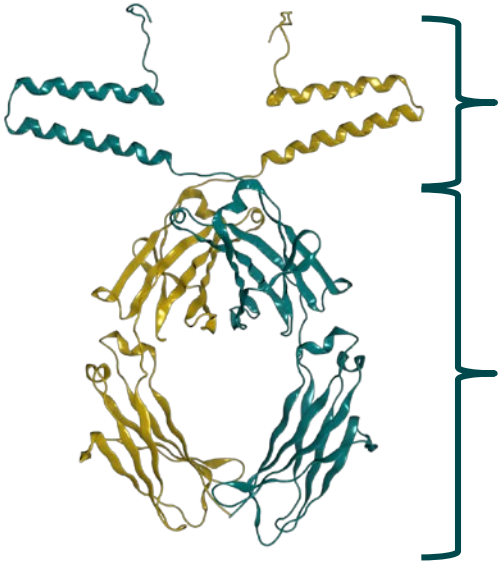
fused to Fc domain of human antibody

iMod Domain of HARS:

- Enriched in the human lung
- Inhibits human T cell activation

Fc Domain of Human Antibody:

- Used to extend half-life
- Once-monthly dosing regimen



Receptor/Mechanism of Action:

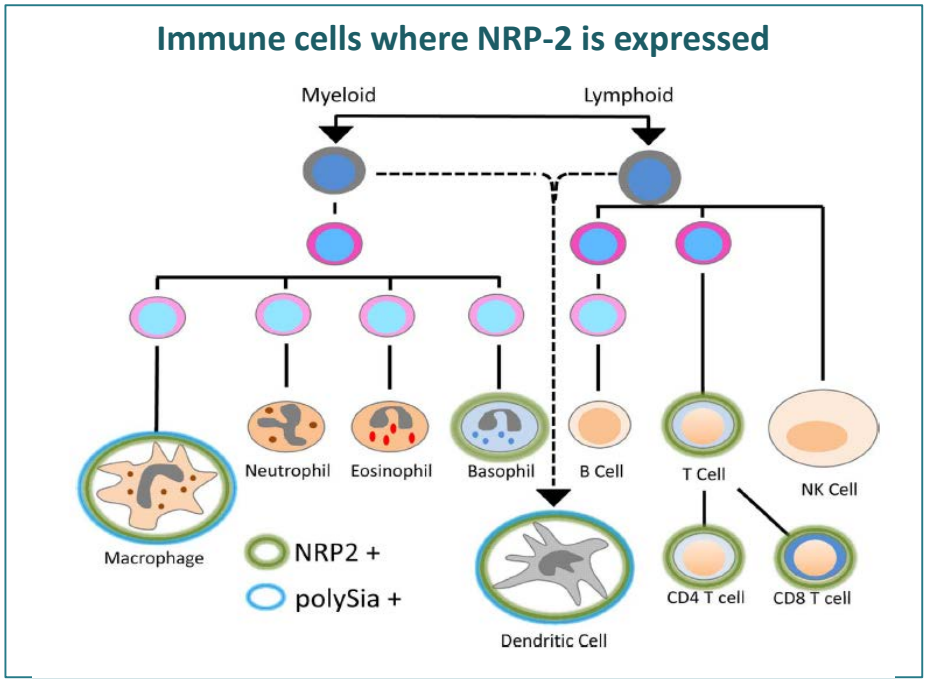
- "iMod domain" binds to Neuropilin-2 (NRP-2)
- Regulates immune system

Receptor: Importance of NRP-2 as a Binding Partner for ATYR1923

- Pleiotropic receptor that can bind to a number of different ligands
- Well-established role in the development of the neural and lymphatic systems

➢ Emerging role in the **immune system**; present on a number of immune cell types

➢ Expressed on alveolar macrophages, may play role in **regulating lung inflammation**



Schellenberg et al. *Role of Neuropilin-2 in the immune system.* Mol. Immunol. 90, 239-244. 2017

NRP-2 Connections to T Cell Biology

Immunomodulatory Effects of Neuropilin-2 On T Cells

H. Nakayama,[1,2] N. Kochupurakkal,[1] S. Bruneau,[1] D. Bielenberg,[2] M. Klagsbrun,[2] D. Briscoe.[1]

[1]Transplant Research Program, Boston Children's Hospital, Boston, MA
[2]Vascular Biology Program, Boston Children's Hospital, Boston, MA.

Meeting: 2015 American Transplant Congress

Abstract number: 139

OPEN ACCESS Freely available online PLOS ONE

Semaphorin 3F and Neuropilin-2 Control the Migration of Human T-Cell Precursors

Daniella Arêas Mendes-da-Cruz[1,2¤], Anne Colette Brignier[1,3¤], Vahid Asnafi[4], Frederic Baleydier[4], Carolina Valença Messias[2], Yves Lepelletier[1,5], Nawel Bedjaoui[4], Amedée Renand[1], Salete Smaniotto[6], Danielle Canioni[4,6], Pierre Milpied[1], Karl Balabanian[8], Philippe Bousso[9], Stéphane Leprêtre[10], Yves Bertrand[11], Hervé Dombret[12], Norbert Ifrah[13], Mireille Dardenne[1], Elizabeth Macintyre[4], Wilson Savino[2], Olivier Hermine[1,4,5]*

Emerging area of immunology

Implicated in multiple organ systems:

- Lung
- Lymphatics
- Smooth Muscle

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 282, NO. 42, pp. 30346–30356, October 19, 2007

SCIENTIFIC REPORTS

OPEN

Regulation of mTOR Signaling by Semaphorin 3F-Neuropilin 2 Interactions *In Vitro* and *In Vivo*

Received: 23 March 2015
Accepted: 04 June 2015
Published: 09 July 2015

Hironao Nakayama[1,2,3,4], Sarah Bruneau[1,5], Nora Kochupurakkal[1,5], Silvia Coma[1,3], David M. Briscoe[1,6,*] & Michael Klagsbrun[1,2,6,*]

Polysialylated Neuropilin-2 Is Expressed on the Surface of Human Dendritic Cells and Modulates Dendritic Cell-T Lymphocyte Interactions*

Received for publication, April 9, 2007, and in revised form, July 24, 2007 Published, JBC Papers in Press, August 15, 2007, DOI 10.1074/jbc.M702965200

Sabrina Curreli[‖], Zita Arany[§], Rita Gerardy-Schahn[¶1], Dean Mann[§], and Nicholas M. Stamatos[‖2]

From the [‖]Institute of Human Virology, University of Maryland, Baltimore, Maryland 21201, [§]Department of Pathology and [‖]Division of Infectious Diseases, Department of Medicine, University of Maryland Medical System, Baltimore, Maryland 21201, and [¶]Zentrum Biochemie, Abteilung Zellulare Chemie, Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany

ATYR1923 for the Treatment of Interstitial Lung Diseases

High Unmet Need in Multiple Interstitial Lung Diseases

Sarcoidosis

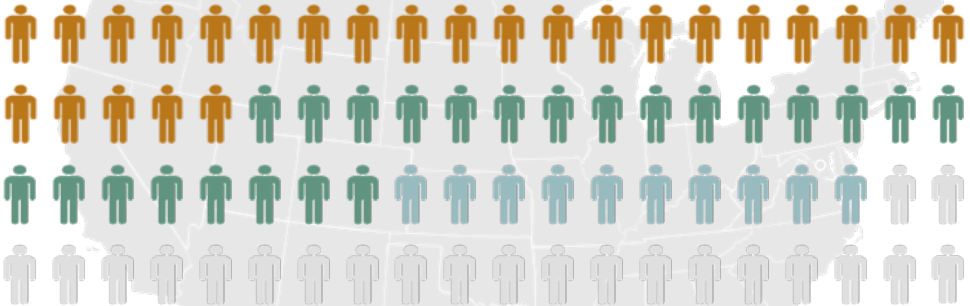
~150K patients in the U.S.

- Systemic inflammatory disorder w/ granulomas
- CD4+ T cell driven
- Advanced pulmonary disease leading cause of death
- ~30% of patients unresponsive to steroid treatment

Chronic Hypersensitivity Pneumonitis (CHP)

~60K patients in the U.S.

- Exaggerated immune response to external antigen
- Commonly misdiagnosed as IPF
- Median survival: 7 years
- No effective therapeutic options



Idiopathic Pulmonary Fibrosis (IPF)

~135K patients in the U.S.

- Irreversible, progressive disease with acute episodes
- Median survival: 3-5 years
- Current SOC: Nintedanib / pirfenidone
  - **Poor G.I. side effect profile**
  - **~$2.0B+ combined sales in 2017 and growing**

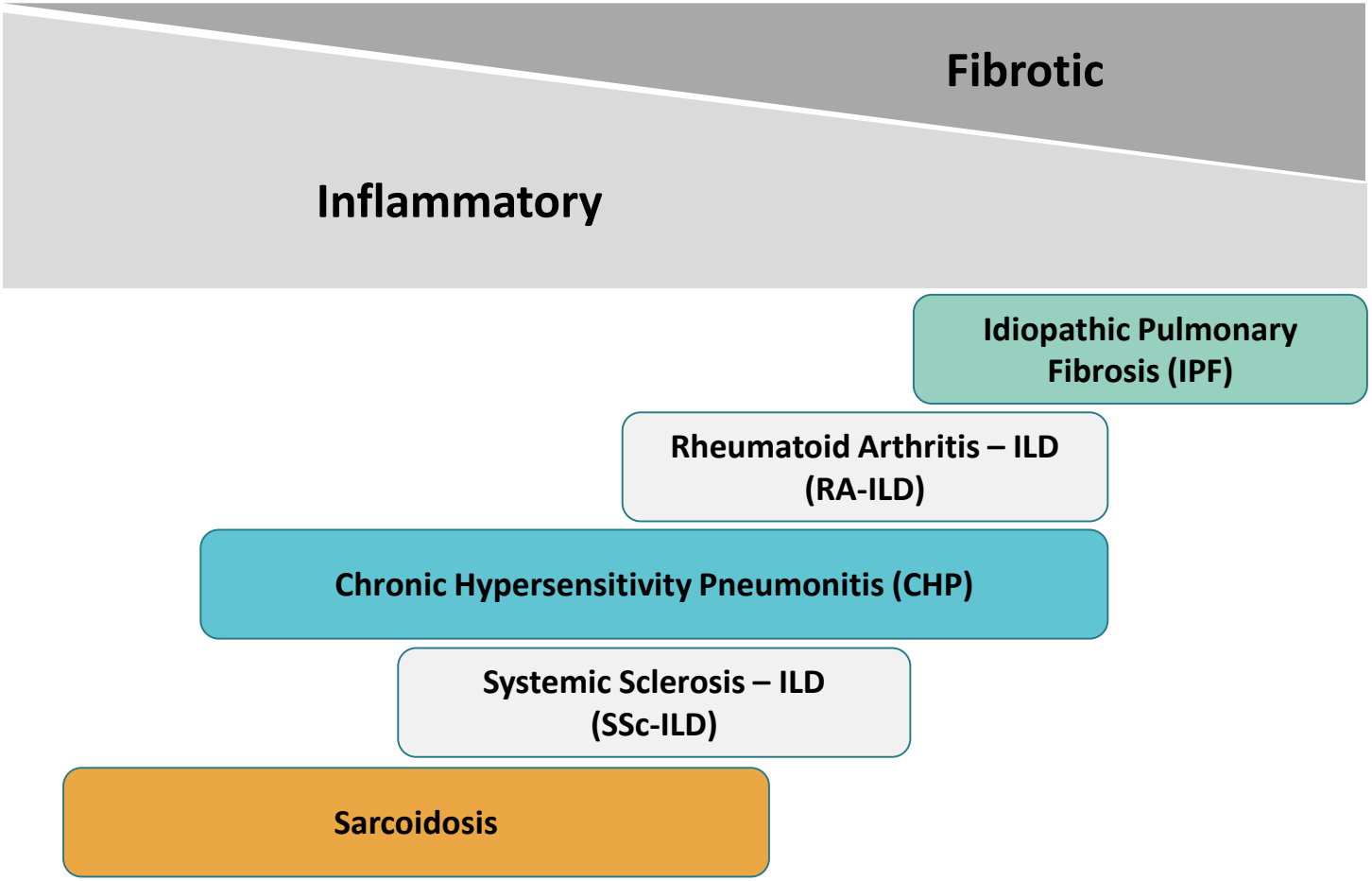
Scleroderma, Rheumatoid Arthritis, & Others (SSc-ILD & RA-ILD)

~250K in other ILDS disorders

- All share underlying inflammatory insult
- Many have grave prognosis
- SOC has limited evidence of safety or efficacy

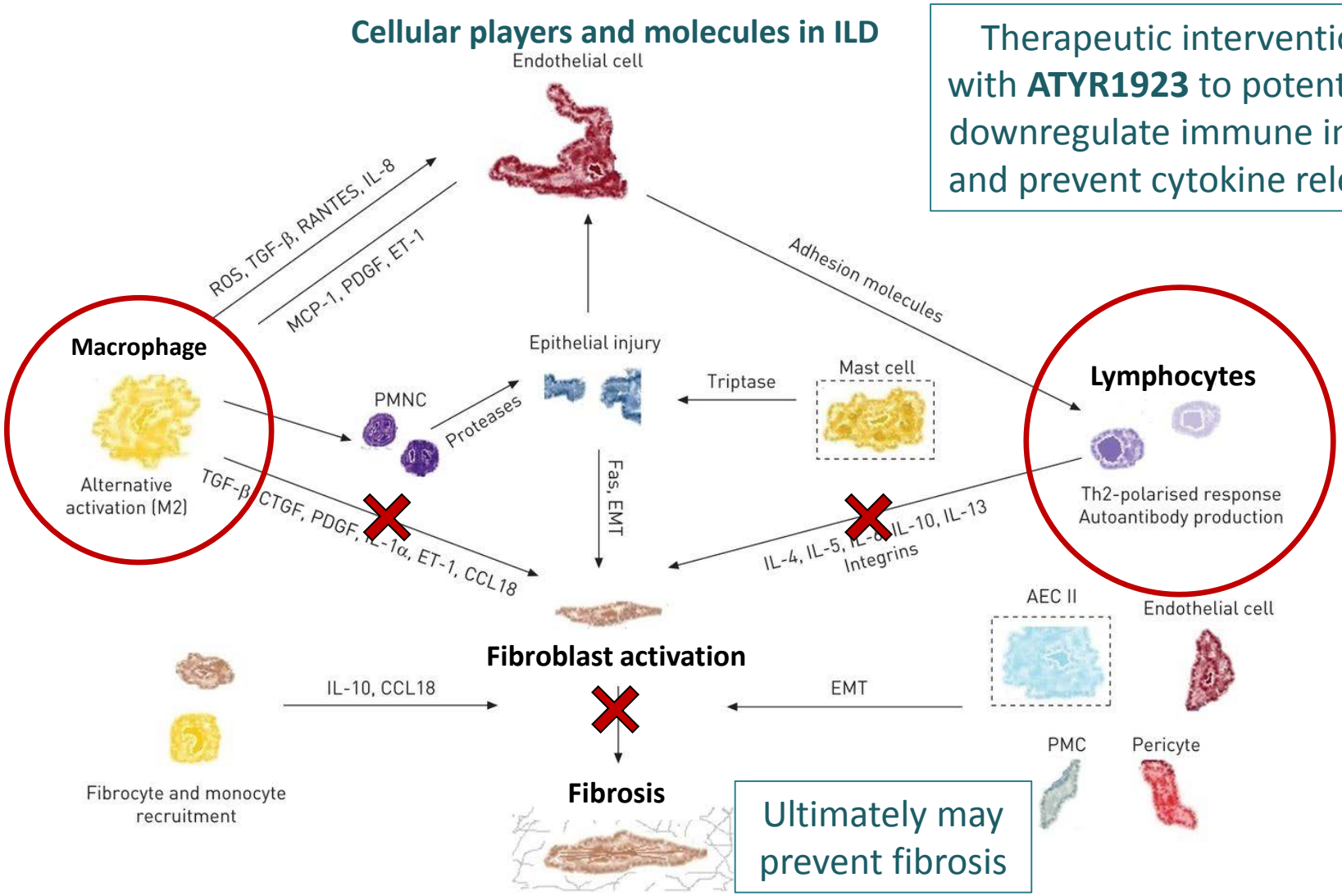
2017 annual sales of Ofev® (nintedanib) ~920 Euros, 52.3% increase YoY
2017 annual sales of Esbriet® (pirfenidone) ~869 CHF, 13% increase YoY

Interstitial Lung Diseases Share Persistent Immune Engagement



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

ATYR1923 Intervention in Interstitial Lung Disease Pathogenesis



Therapeutic intervention with **ATYR1923** to potentially downregulate immune insult and prevent cytokine release

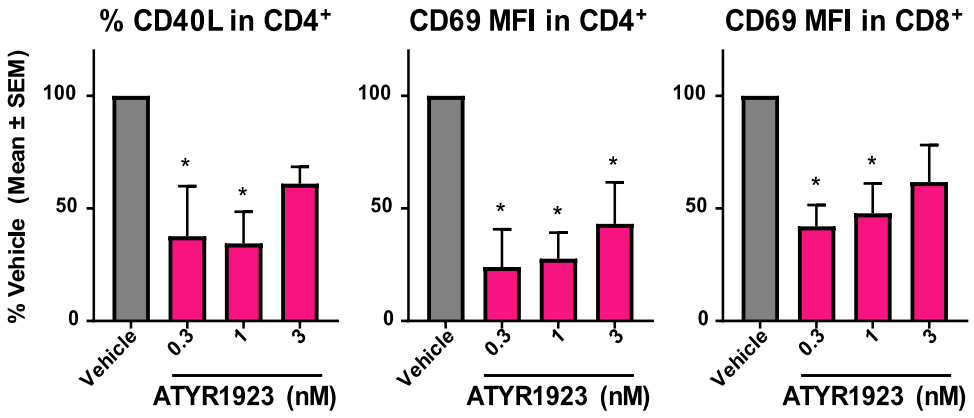
Ultimately may prevent fibrosis

Bagnoto, Harari, *European Respiratory Review*, 2015

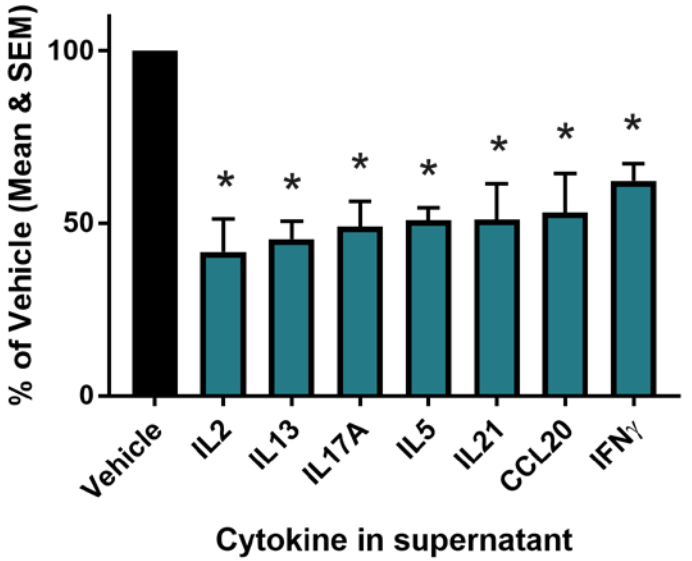
aTyr Pharma NASDAQ: LIFE

Mechanism of Action: ATYR1923 Inhibits T Cell Activation In Vitro

Effect of ATYR1923 on T Cell Activation Markers



Effect of 0.3 nM ATYR1923 on T Cell Cytokine Release



Mean response from 3 donors

aTyr is currently exploring the interaction with ATYR1923 and NRP-2 across multiple immune cell types

*$P < 0.05$

Note: *Presented in a poster at the American Academy of Immunology Annual Meeting in May 2018*

Pre-Clinical Translational Estate Supports Clinical Development in ILD

1923 Provides Therapeutic Activity in Bleomycin-induced Lung Fibrosis Model

- Mouse model comparing pirfenidone* vs. dexamethasome vs. ATYR1923
- 1923 was efficacious and ameliorated lung fibrosis
- Presented at ATS, May 2017

1923 Improves Lung Function in Model

- Rat model comparing nintedanib** vs. ATYR1923
- 1923 was efficacious in additional bleomycin-induced lung fibrosis
- Presented at ATS, May 2018

1923 Ameliorates Dermal and Pulmonary Fibrosis in Model

- Mouse model comparing nintedanib** vs. ATYR1923
- 1923 has robust activity when treatment initiated early (day 7)
- Presented at Scleroderma Foundation Patient Conference, July 2018

*2017 annual sales of Esbriet® (pirfenidone) ~869 CHF, 13% increase YoY

**2017 annual sales of Ofev® (nintedanib) ~920 Euros, 52.3% increase YoY

Phase I: Healthy Volunteer Study

Randomized, double-blind, placebo-controlled, single ascending dose (N=36 HVs)

Positive Phase 1 Data Announced in June 2018:

- ATYR1923 was generally well-tolerated with no significant adverse events
- PK profile supports the potential for a once-monthly dosing regimen

Phase 1 Study Design:

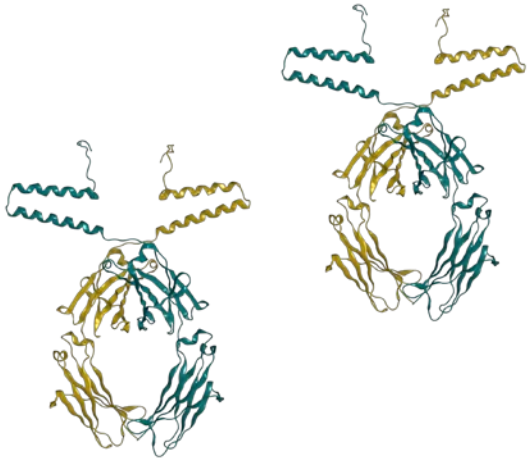
First-in-Patient Trial

Preliminary Design:

- Phase 1b/2a multiple-ascending dose, placebo controlled, first-in-patient study
- Evaluate safety, tolerability and immunogenicity of multiple doses of 1923
- Evaluate clinical activity and potential biomarkers

Upcoming Milestones:

- ❑ Announce Phase 1b/2a specific indication and final protocol
- ❑ Initiate trial in 4Q 2018



Mission to Generate Value for Shareholders and Patients

- ✓ aTyr owns the potential pipeline derived from 20 tRNA synthetase genes
- ✓ *In-vitro* and *in-vivo* studies support clinical development in ILD
- ✓ HARS-based therapeutics safety profile includes 92 subjects
- ✓ Identification of NRP-2 receptor for ATYR1923 elucidates greater understanding of MOA
- ❑ Goal is to clearly show meaningful clinical activity in 1923 patient trial

THANK YOU