aTyr Pharma
NASDAQ: LIFE

Translation of New Immune Pathways into Meaningful Medicines

Cowen and Company 38th Annual Health Care Conference
March 12, 2018

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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 ATYR1940 (Resolaris™), ATYR1923 (iMod.Fc) and our ORCA program, 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, our projected cash expenditures, 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 Quarterly Report on Form 10-Q, our Annual Report on Form 10-K 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.

Accelerating Value Creation from Novel Immune Pathways

Research:

Discover innovative therapeutic candidates based on extracellular functionality of tRNA synthetases

Initial focus on Resokine Pathway

Development:

ATYR1923 (interstitial lung diseases) in ongoing Phase 1 trial

ORCA antibody program (immuno-oncology) in IND enabling activities

Financials:

2017 year-end cash and investments at $85.1M*

Cash runway into 3Q 2019

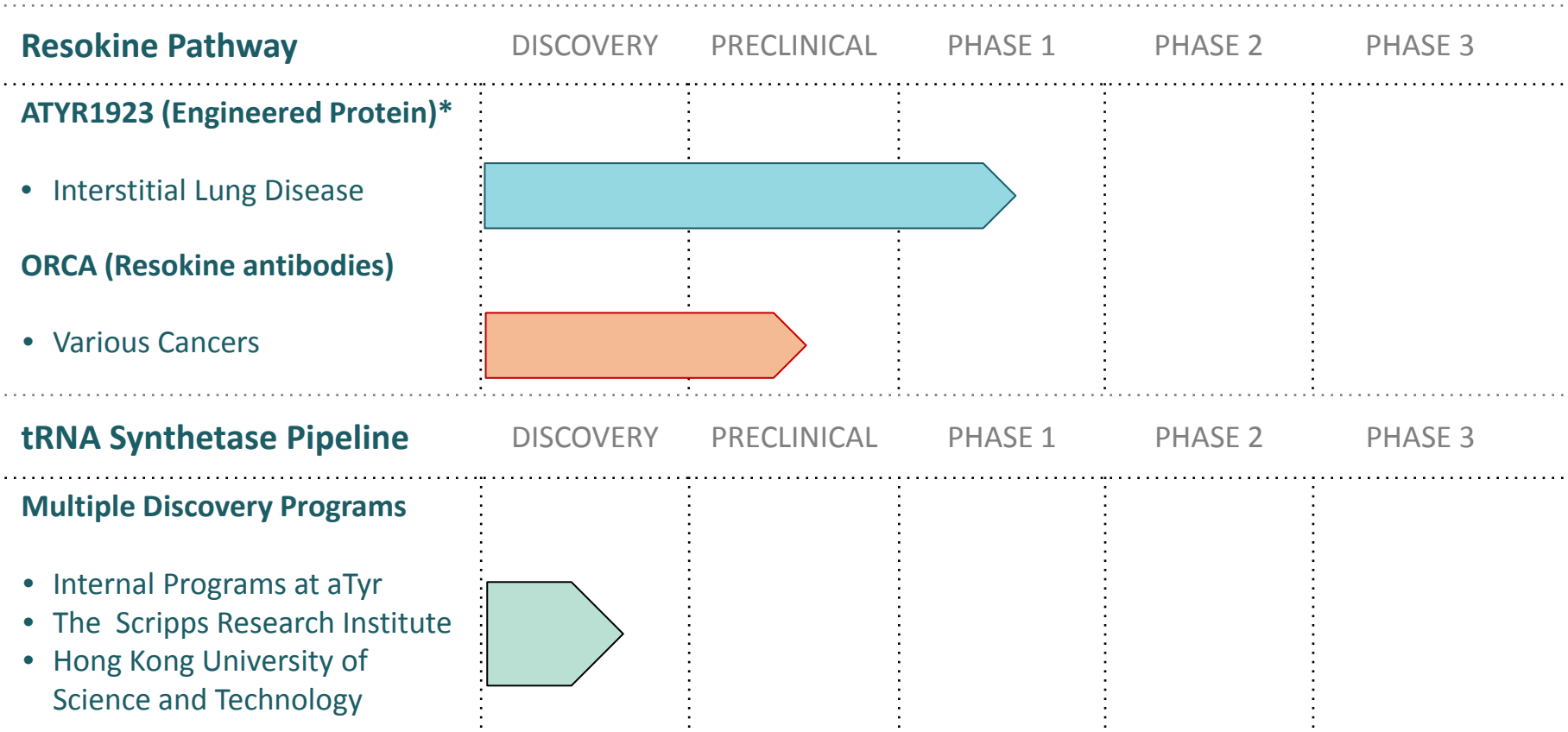
Upcoming Catalysts:

ATYR1923 Phase 1 data – 2Q 2018

ORCA data/posters at AACR in April, 2018

**Estimated cash, cash equivalents, and investments provided pending completion of year-end financial close and external audit*

Therapeutic Candidate Pipeline



ATYR1923 (Engineered HARS): Engineered fusion protein with histidyl-tRNA synthetase (HARS) splice variant (additional information on slide 9)

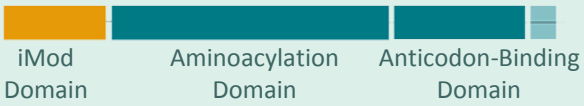
Resokine: Extracellular Proteins Derived From HARS Gene

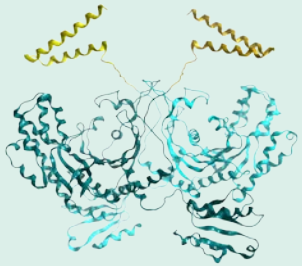
tRNA Synthetase Genes:

AARS
CARS
DARS
EPRS
FARS
GARS
HARS
IARS
KARS
LARS
MARS
NARS
QARS
RARS
SARS
TARS
VARS
WARS
YARS

Intracellular:
(Cytoplasm)

Histidyl-tRNA Synthetase
509 AA
Function: Protein synthesis

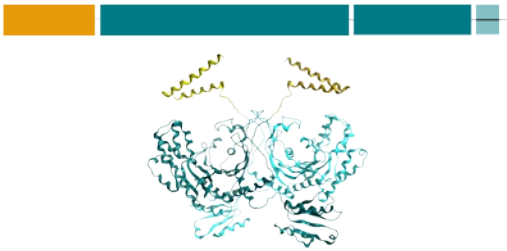




Secretion

Extracellular: Resokine Pathway
(Circulation)

Resokine
Full length HARS: 509 AA
Function: Immunomodulation



N-terminal iMod domain
iMod domain (SV9): 59 AA
Function: Immunomodulation

aTyr has built an intellectual property estate, to protect its pipeline, comprising over 300 potential protein compositions derived from all 20 human tRNA synthetase genes.

Resokine MOA Hypothesis: Regulates T Cell Activation

Acts on both CD4 and CD8 T cells

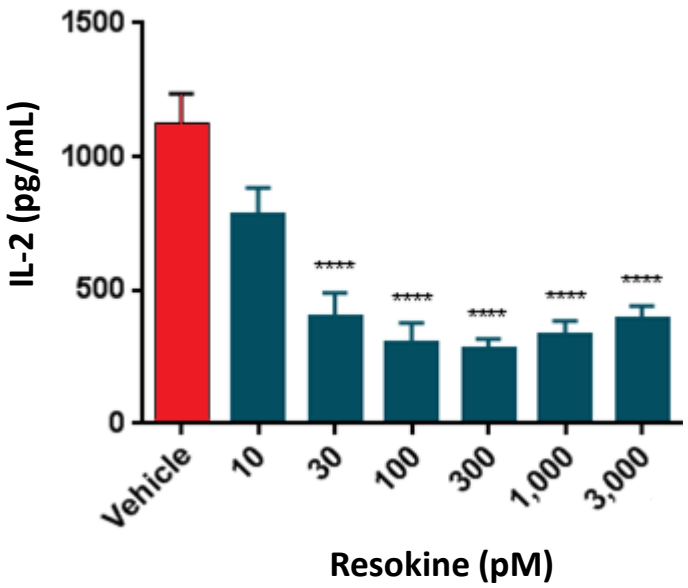
Effector functions at levels closer to a resting T cell

Stimulatory pathways at levels closer to a resting T cell

Shifts trafficking and residence closer to a resting T cell

Resokine Regulates T Cell Activation

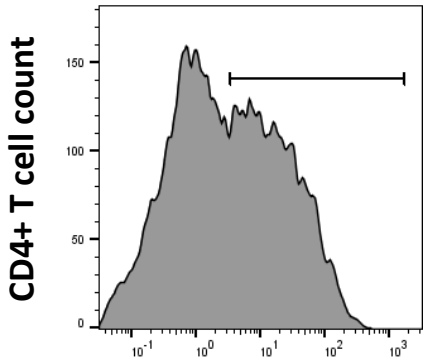
Human T Cell IL-2 Release Post Activation



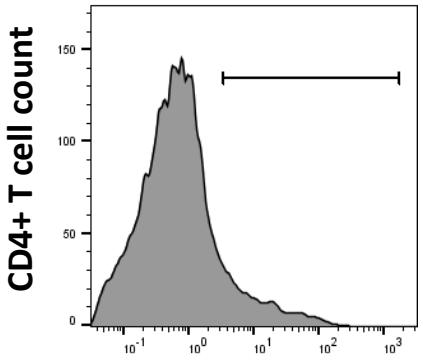
**** $p < 0.0001$

Similar for: INFγ, TNFα…
Similar to hitting PD-1 pathway

Anti-CD3/CD28 (24 hr.) Stimulation + Vehicle

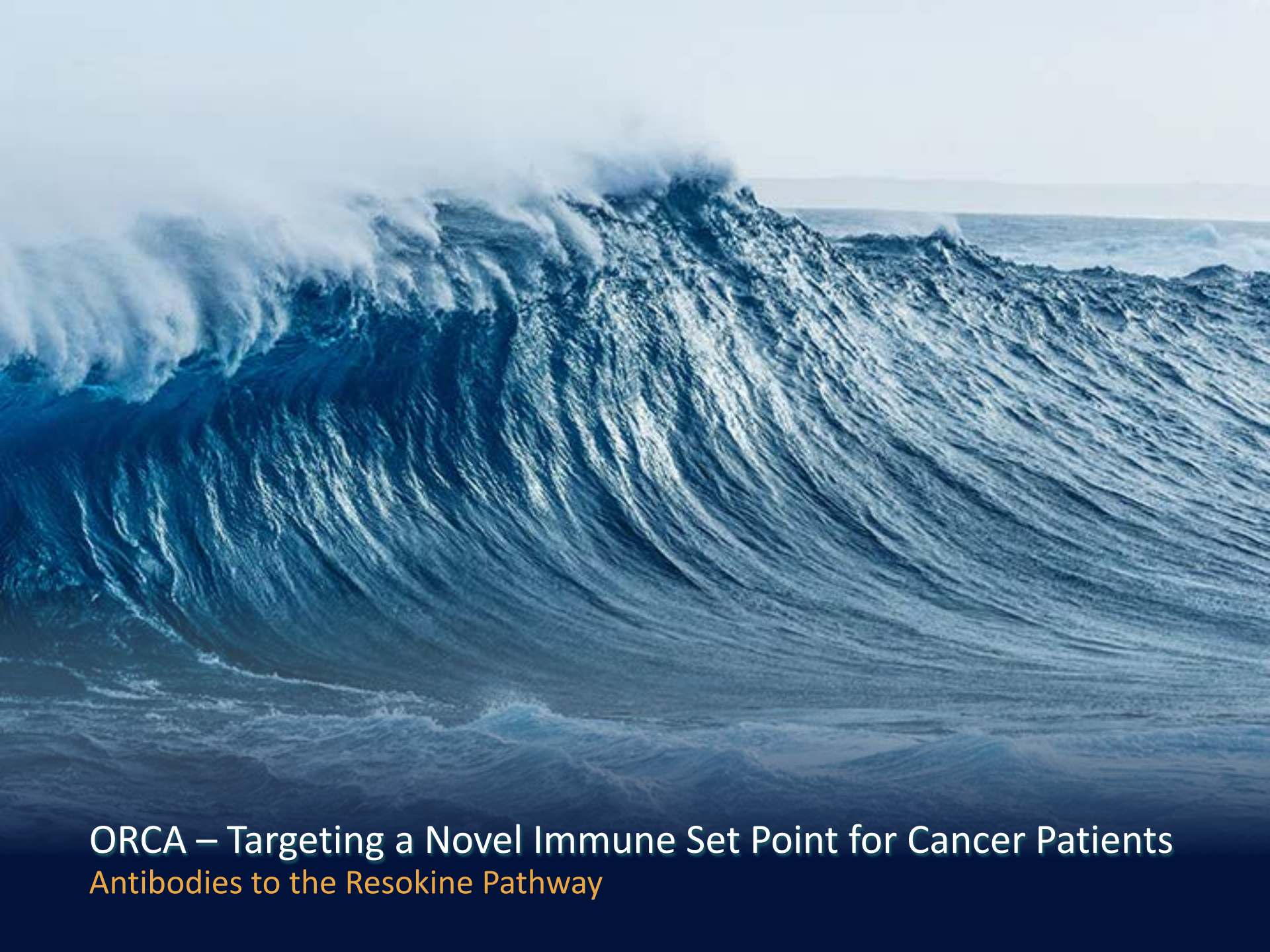


Anti-CD3/CD28 Stimulation + Resokine (100pM)



Similar for:
CD69, 4-1BB,
PD-1, ICOS…

Graphs on Right: *T cells were stimulated with anti-CD3/CD28 antibodies in the presence of vehicle or Resokine. After 24 hours, supernatants were collected and analyzed by ELISA. Statistics by T test.*

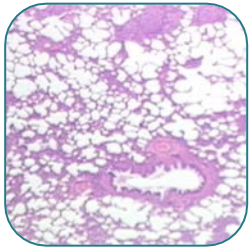


ORCA – Targeting a Novel Immune Set Point for Cancer Patients

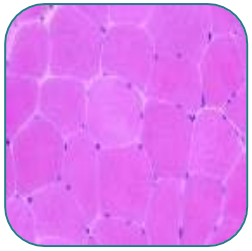
Antibodies to the Resokine Pathway

Anti-Synthetase Syndrome: Resokine Disruption via Auto-Antibodies

Healthy Tissue



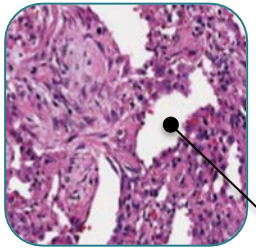
Healthy lung



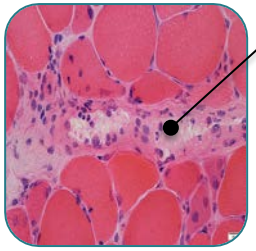
Healthy muscle

Resokine disruption via auto-antibodies

T Cells Mobilized in Tissue

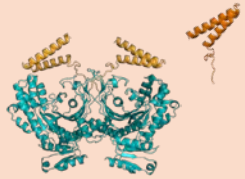


Interstitial Lung Disease

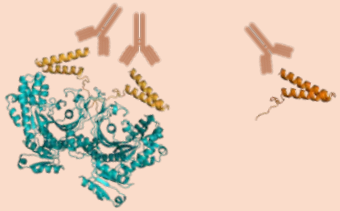


Inflammatory Myopathy

↑ Immune cell invasion/activity



Resokine acts as regulator of immune activity



Antibodies to Resokine lower threshold for T cell activation

**100% (18 of 18) anti-synthetase syndrome patients tested positive for antibodies for Resokine proteins*

ORCA Program: Snapshot

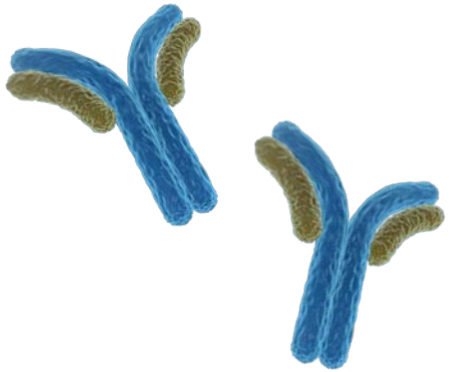
Patients:
Potentially all cancer types:

- >450 patient samples in 15 tumor types tested
- ~95% of cancer patients tested positive for Resokine

Target:
Resokine pathway

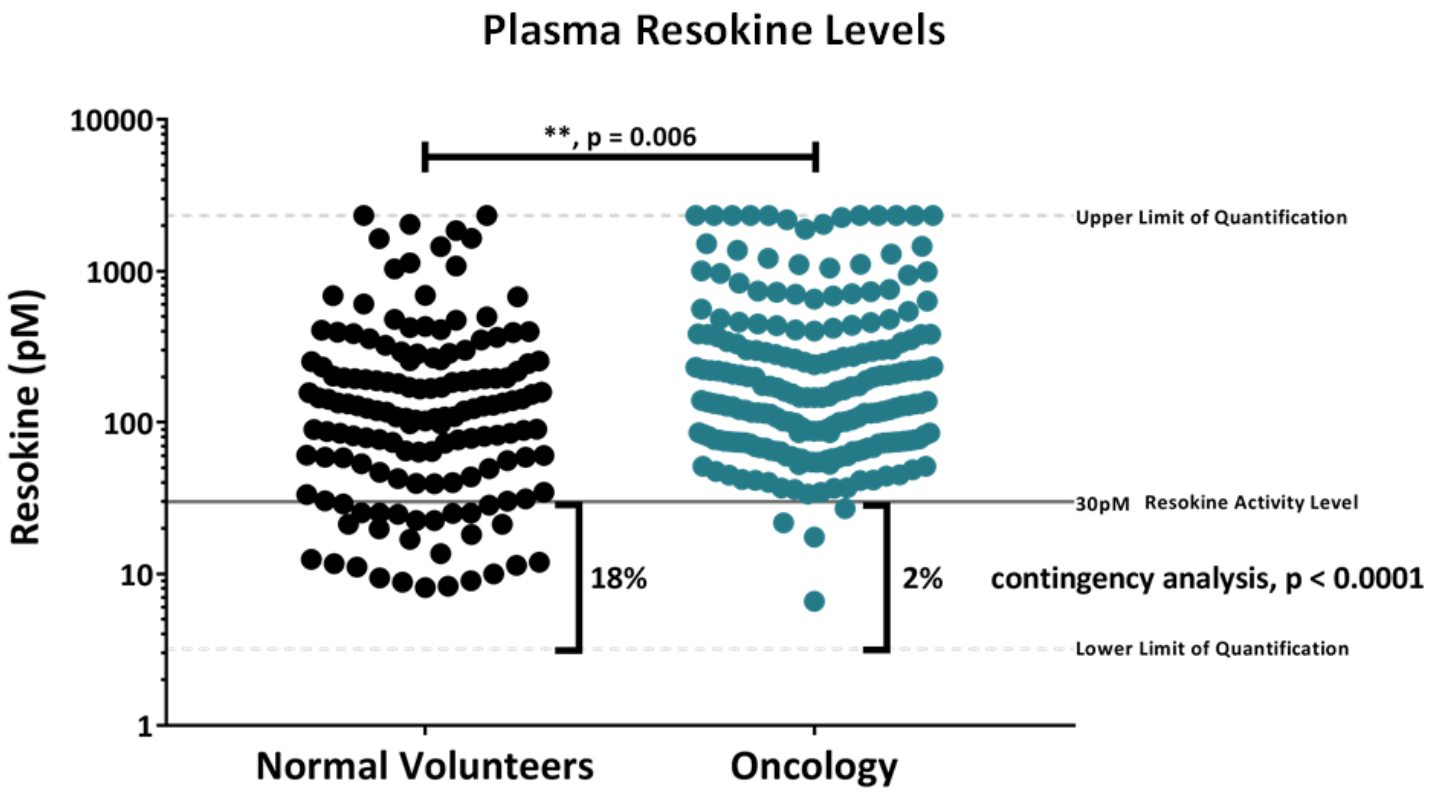
Therapeutic Concept:
Antibody to block Resokine activity, increases T cell engagement

Rationale:
Human evidence of Resokine antibody changing T cell behavior (anti-synthetase syndrome patients)
Phenotype replicated in animal functional knock-out models



Biomarker:
Liquid biopsy correlates with tumor volume and efficacy

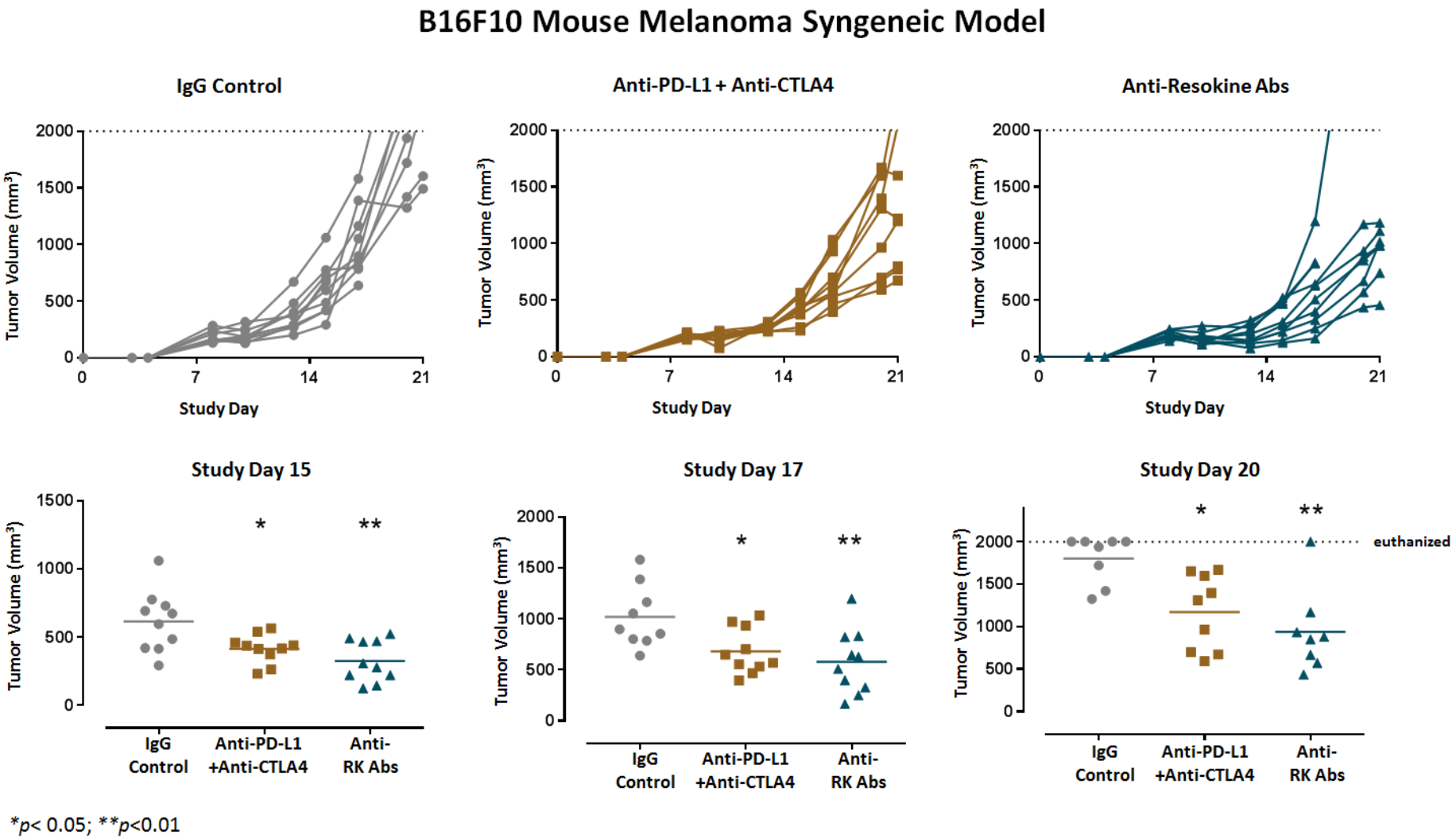
Cancer Patients Have Higher Plasma Resokine Levels



Plasma; Resokine ELISA; NHV: n=148; Oncology: n=215; Mann-Whitney

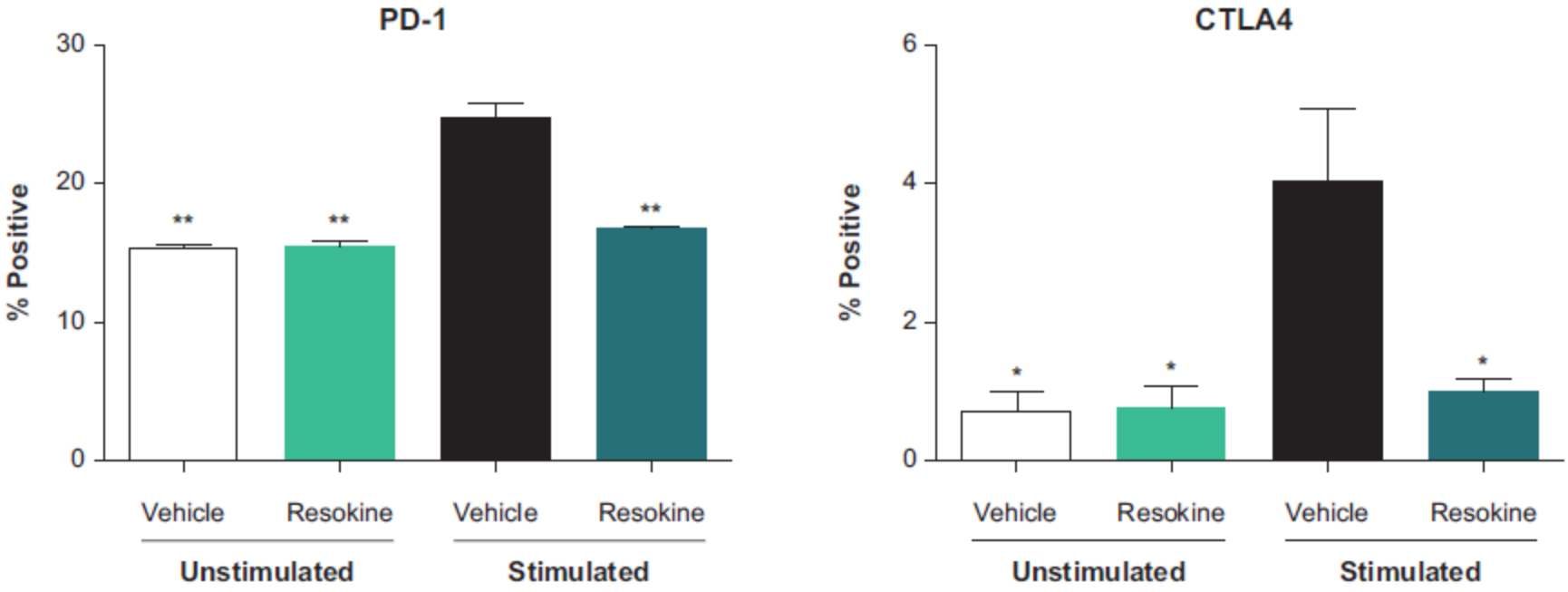
Note: *Presented in a poster at the ASCO-SITC conference in January 2018*

Anti-Resokine Antibodies Have Anti-Tumor Activity



Note: *Presented in a poster at the ASCO-SITC conference in January 2018*

Resokine Inhibits Up-regulation of PD-1 and CTLA-4



Human T cells, 24h unstimulated, stimulated (CD3/ CD28) 24 h + Resokine @ 1 nM

Note: *Presented in a poster at the ASCO-SITC conference in January 2018*

ORCA Program: Supportive *In Vivo* Data and Development Timelines

In Vivo Efficacy Data

Resokine Abs effective in multiple mouse syngeneic tumor models

- ✓ Outperformed checkpoint inhibitors (e.g. Abs to PD-1, PD-L1, CTLA-4) in various animal models

Resokine Abs effective alone and in combination

- ✓ Efficacy potential as monotherapy and with checkpoint inhibitors (based on tumor model data)

Development Timelines

Resokine antibody selection:

- ✓ Panel of antibodies selected and in IND enabling activities

Present Data at Scientific Conferences:

- ✓ Abstract at ASCO-SITC in January 2018
- ✓ ORCA posters at AACR in April, 2018

First clinical trial in patients:

- ❑ Initiate in 2019

ATYR1923 for the Treatment of Interstitial Lung Diseases

Engineered HARS Splice Variant

ATYR1923: Program Snapshot

ATYR1923:

Engineered fusion protein with HARS splice variant

Refer to splice variant as the "iMod domain"

(iMod for **i**mmuno-**mod**ulatory function)

Patients:

Interstitial lung diseases (ILDs) characterized by an immune component

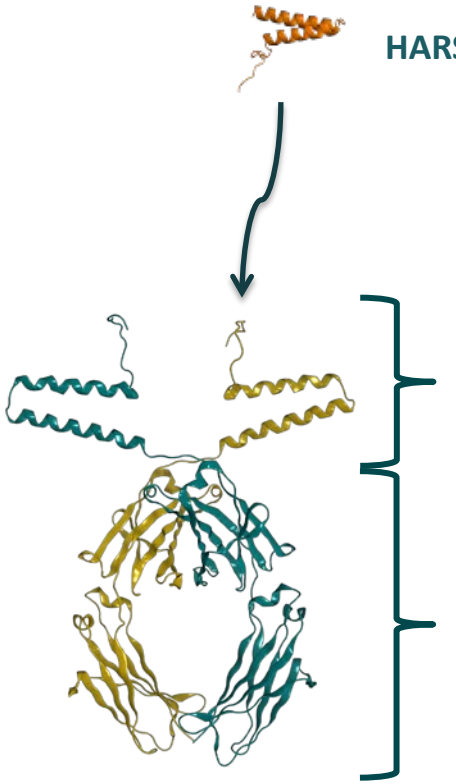
Mechanism:

Regulation of T cell activation via the Resokine pathway

Rationale:

Functional knockout of Resokine pathway in humans and rodents results in T cell mobilization and lung damage

Immune dysfunction is key to pathophysiology of ILDs



Target Dosing:

Improved pharmacokinetic profile that supports once/twice monthly IV infusion

Interstitial Lung Diseases Share Persistent Immune Engagement

Idiopathic Pulmonary Fibrosis (IPF)

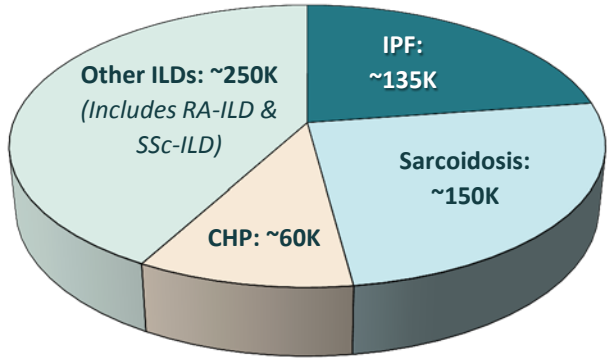
Rheumatoid Arthritis – ILD (RA-ILD)

Chronic Hypersensitivity Pneumonitis (CHP)

Systemic Sclerosis – ILD (SSc-ILD)

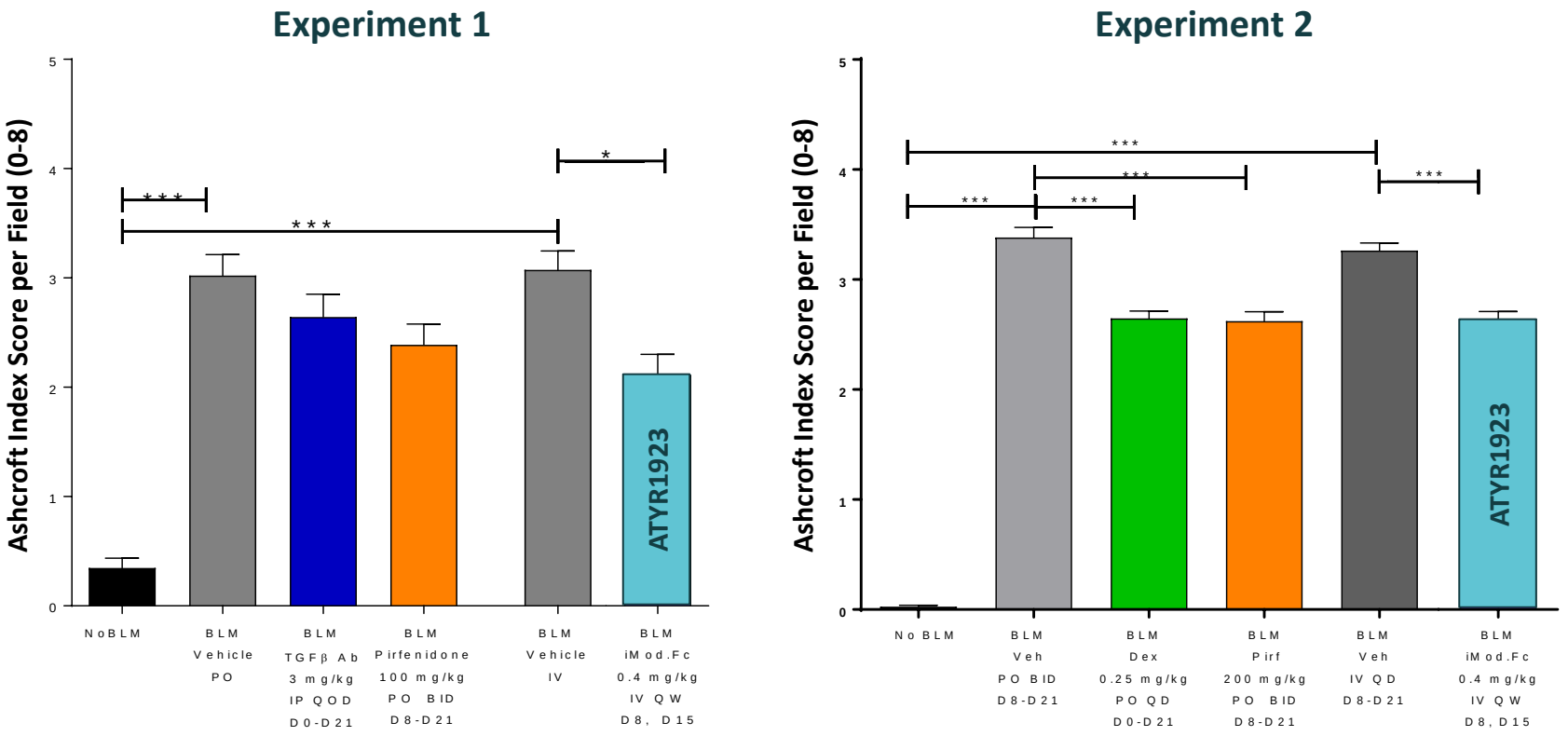
Sarcoidosis

Estimated ILD US Patient Populations



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

ATYR1923 Ameliorates Fibrosis in Bleomycin-Induced Lung Injury



ATYR1923 (iMod.Fc) administered therapeutically at 0.4 mg/kg weekly drives efficacy comparable to or greater than Pirfenidone*, anti-TGF antibodies, and dexamethasone

Pirfenidone: *Current approved therapy for IPF patients (annual sales in 2016 ~ $830M)*

Note: *Presented in a poster at the American Thoracic Society in May 2017*

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ATYR1923 Clinical Development for Interstitial Lung Diseases

Clinical Overview
Randomized, double-blind, placebo-controlled studies to investigate the safety, tolerability, immunogenicity, pharmacokinetics and pharmacodynamics of intravenous ATYR1923 (iMod.Fc) in healthy volunteers and patients with interstitial lung disease.

Phase 1 - Healthy Volunteers:
- 36 subjects across 6 dose cohorts
- Dosing (single infusion):
  - 0.03 mg/kg up to potentially 5.0 mg/kg

✓ First subjects dosed in the fourth quarter of 2017
❑ Data expected in 2Q 2018

Phase 2 - Interstitial Lung Disease patients with an immune component:
- Collaborating with industry leading clinicians to develop patient trials for ATYR1923

Accelerating Value Creation from Novel Immune Pathways

2018 Strategic Goals:

Advance Clinical Development

- ATYR1923 Phase 1 ongoing with data in 2Q 2018

Advance Immuno-Oncology Program

- IND-enabling activities ongoing for patient trials in 2019

Discovery and Pipeline Enhancement

- Collaborating with academic institutions and ongoing internal programs to discover innovative therapeutic candidates from tRNA synthetase biology

Financials:

✓ **$85.1M*** cash and investments as of 12/31/17; cash runway into 3Q 2019

✓ Market capitalization as of closing price on 3/05/18: ~**$123M****

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**Estimated cash, cash equivalents and investments provided pending completion of year-end financial close and external audit*
***Market capitalization calculated using all common shares outstanding and preferred class X shares on an if-converted basis for a total outstanding share count of 41.14M shares.*