



Targeting Novel Immune Therapeutic Intervention Points

Leveraging a New Pathway in Immunology to Treat Cancer
and Immune-mediated Diseases

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LIFE Investment Highlights

1. Discovered New Pathway in Immunology: Resokine

- IP estate includes over 220 issued patents or allowed patents that are owned or exclusively licensed

2. First Two Clinical Applications of Resokine Pathway Focus on Muscle & Lung

- Resolaris for the treatment of Rare Myopathies with an immune component
- iMod.Fc for the treatment of Interstitial Lung Diseases with an immune component

3. Antagonist Program to Resokine Pathway to Treat Cancer

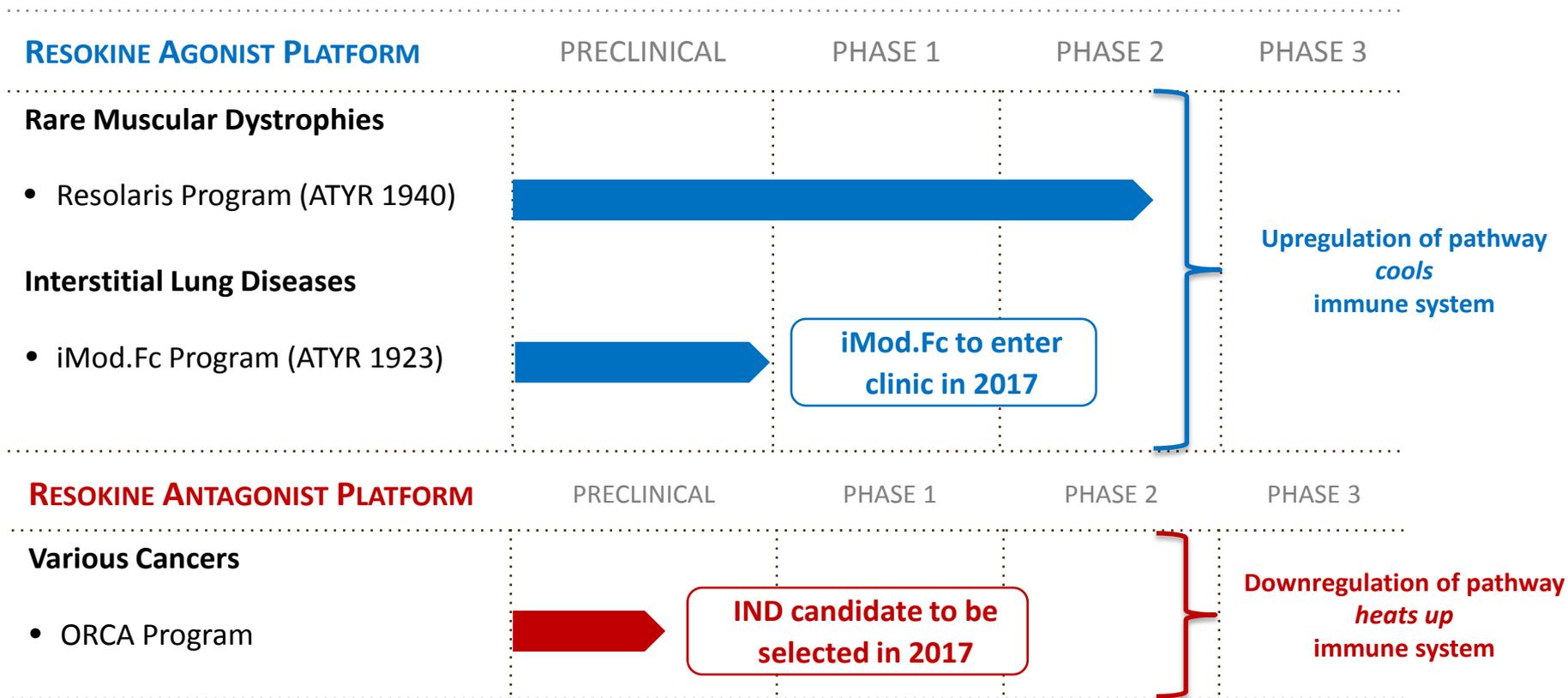
- Potential new universal backbone in immuno-oncology

4. Strengthened Balance Sheet:

- Announced Private Placement on 8/28/17 with **\$45.8M** in gross proceeds
- Financing led by Viking Global Investors, EcoR1, and Redmile Group

LIFE Candidate Pipeline

All programs currently wholly-owned



Resokine Pathway Hypothesis:

A homeostatic pathway that controls the set point of key cells in the immune system.
(*Reso* for resolution; *Kine* for activity)

TAPPING THE POWER OF THE RESOKINE PATHWAY

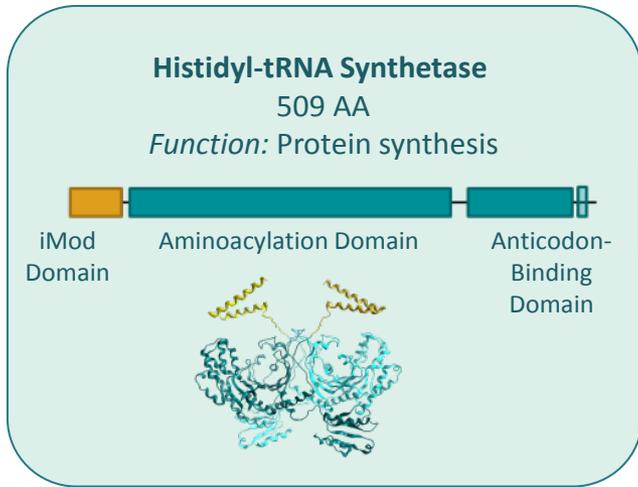
NOVEL PATHWAY IN IMMUNOLOGY EVOLVED OVER 400 MILLION YEARS



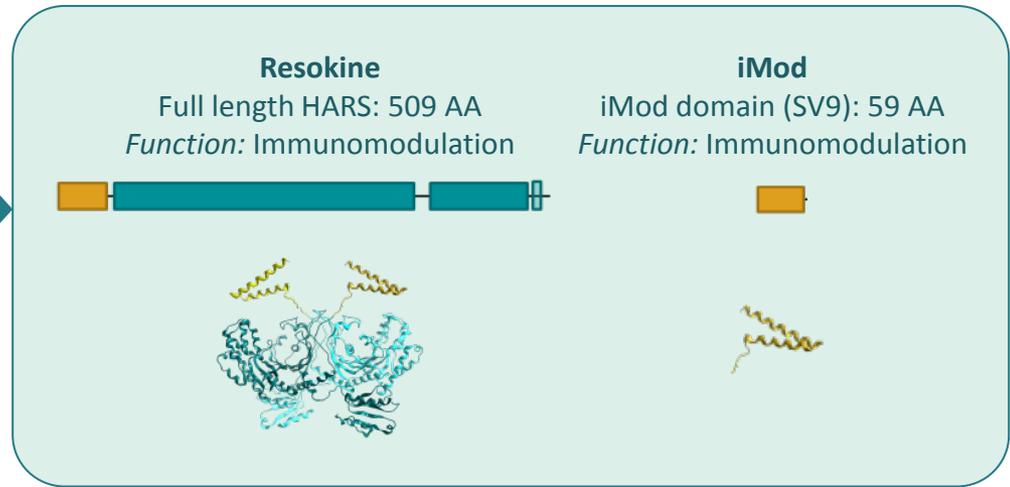
Resokine Pathway

Novel, Primal, Extracellular Signaling Regions in Circulation

Intracellular (Primordial Function)



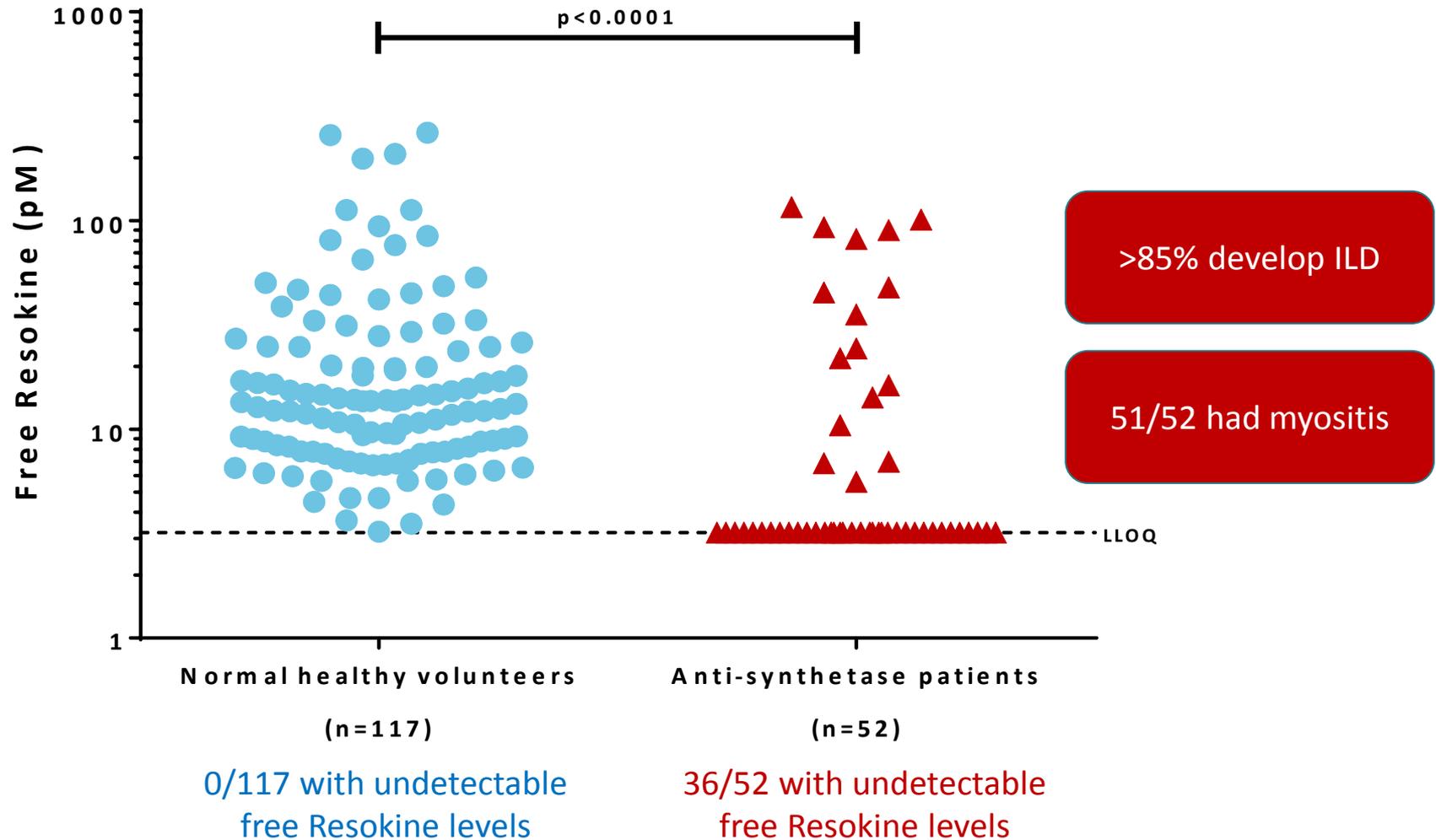
Extracellular (Naturally Occurring In Circulation)



Non-canonical secretion similar to IL-1 or FGF

Nature 2010 Nature 2013 Science 2014

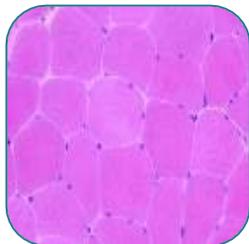
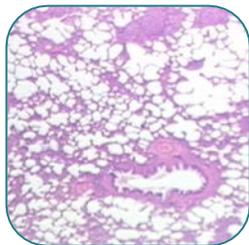
Low Free Resokine Levels in Anti-Synthetase Patients Consistent with Modulatory Hypothesis



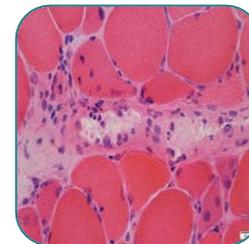
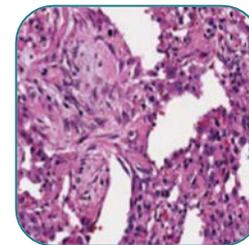
Evidence For A New Immunological Pathway in Humans

Disrupting Resokine Pathway Promotes T Cell Invasion and Disease

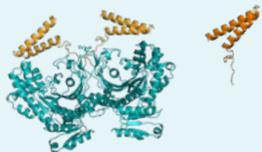
Healthy Tissue



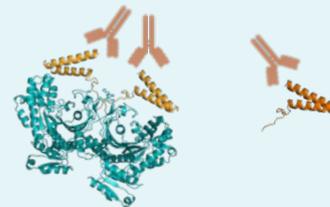
Lung and Muscle Disease



Resokine Pathway

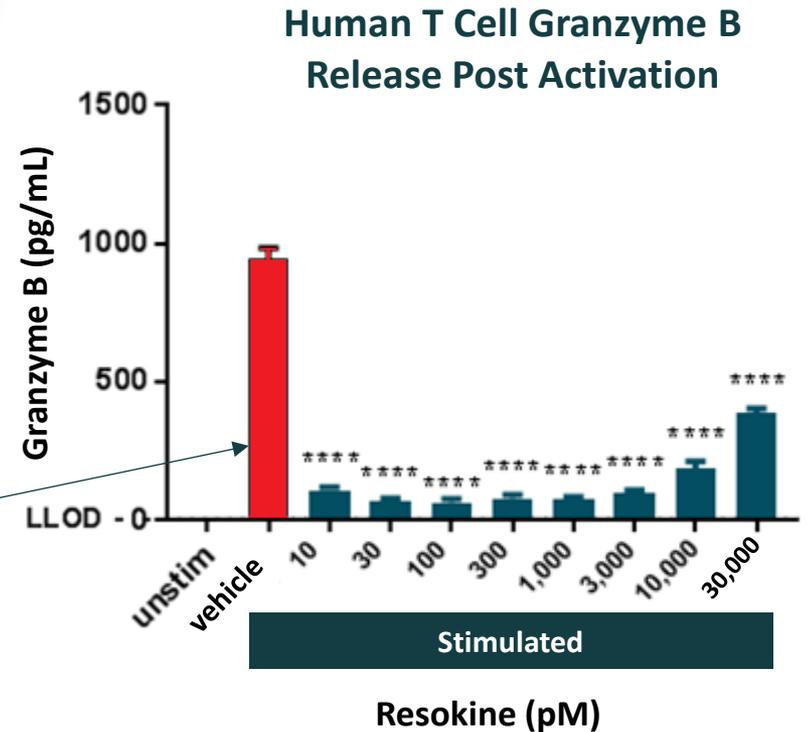
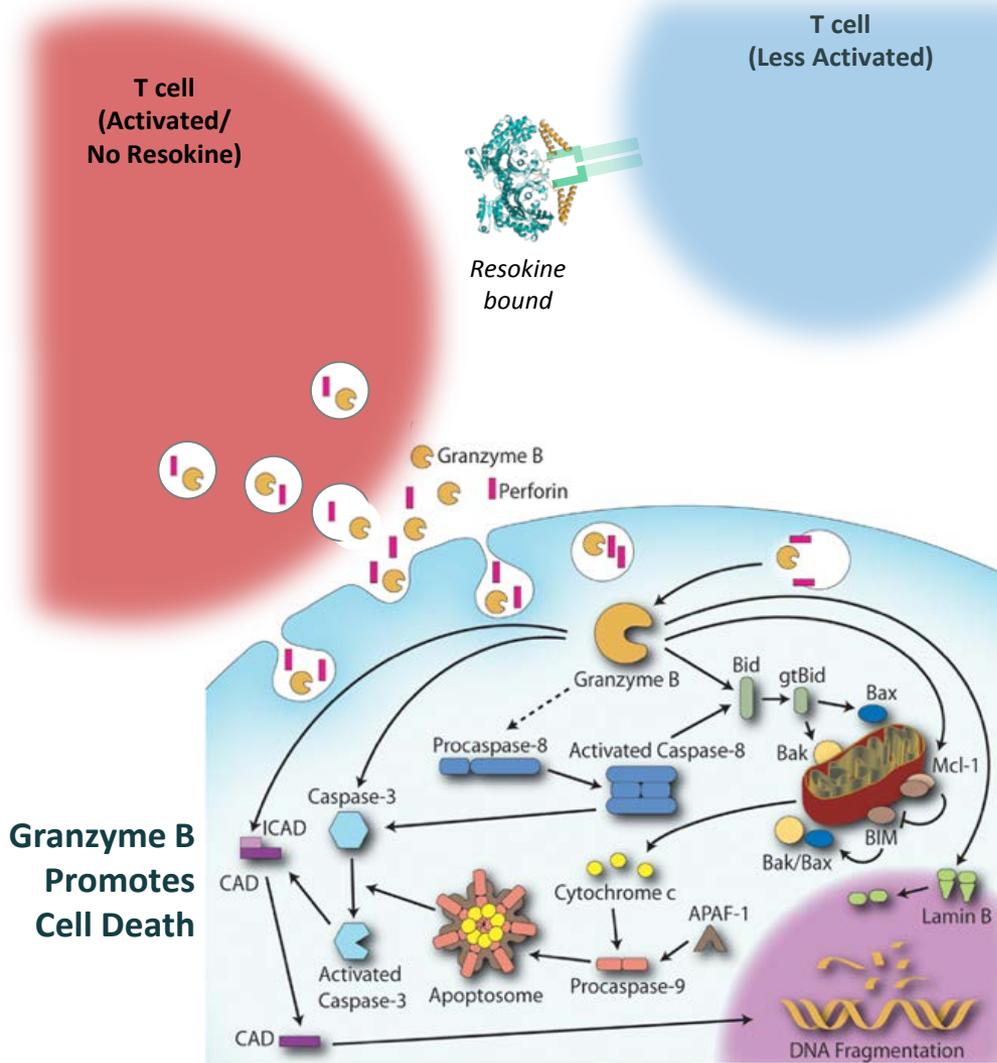


Resokine modulates immune system to promote homeostasis



Antibodies to Resokine antagonize modulation promoting disease

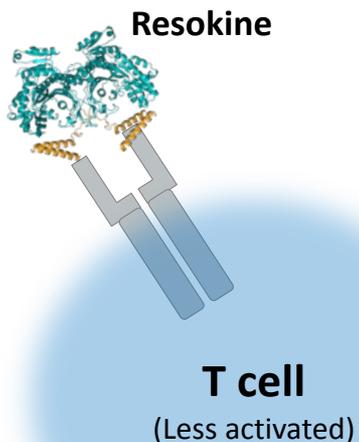
MOA Hypothesis: T Cells Release Granzyme B That Promotes Cell Death & Local Tissue Damage



Note: Common with human donors and T cell assays to have variability

Resokine Agonists Change T Cell Phenotype

Unique MOA to orchestrate immune homeostasis in activated T cells



Acts predominantly on CD4 & CD8 (activated only)

Effector functions at levels closer to a resting T cell

Stimulatory pathways at levels closer to a resting T cell

Shifts trafficking & residence closer to a resting T cell

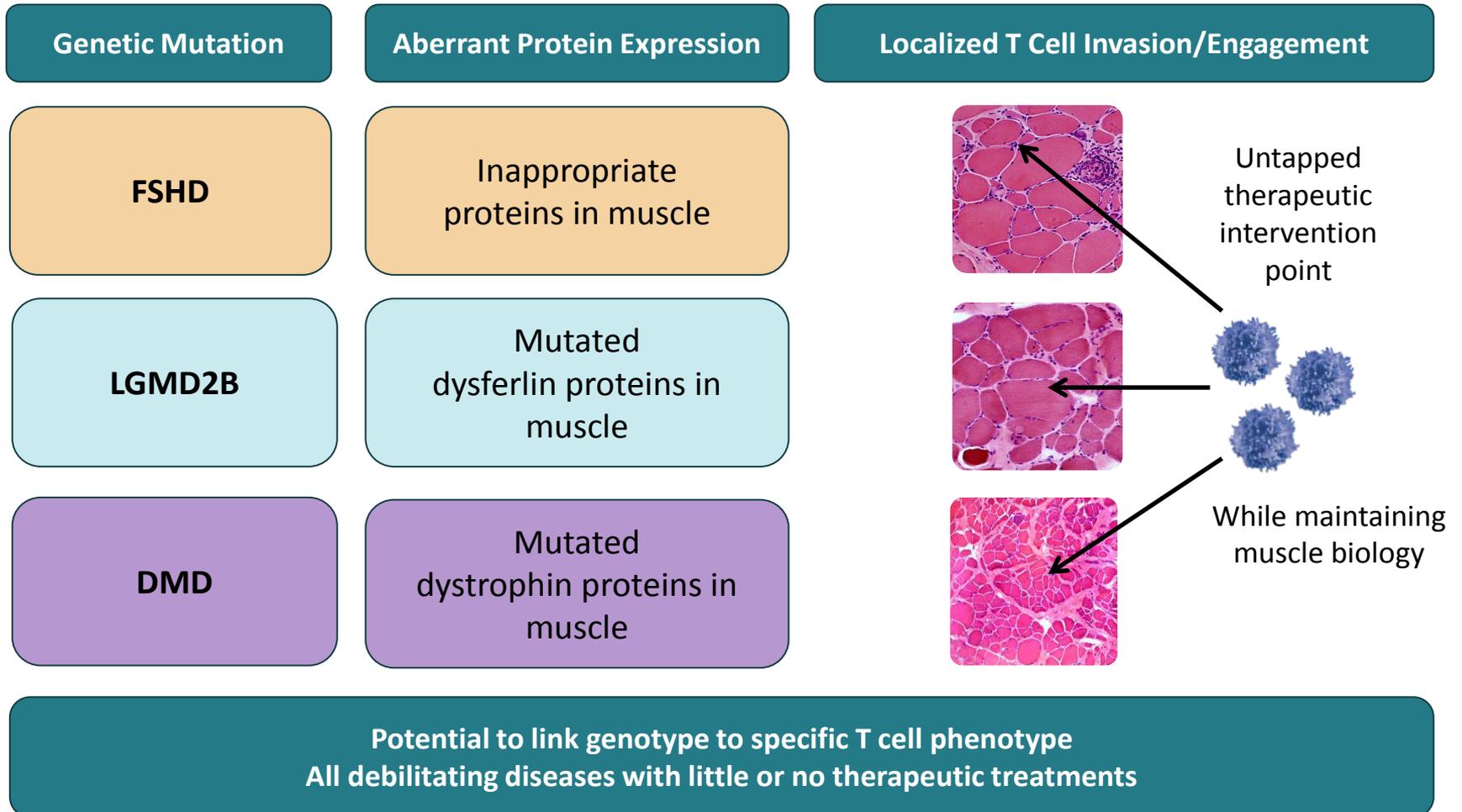


RESOLARIS PROGRAM

**HARNESSING THE RESOKINE PATHWAY
TO TREAT MULTIPLE RARE MUSCLE DISEASES**

Rare Myopathies Have an Immune Component

Chronic damage, homeostasis disrupted



Resolaris Program Snapshot

Patients:

Rare Muscular Dystrophies
with an immune component

Therapeutic Concept:

Resokine normally secreted by skeletal muscle
Upregulate naturally occurring homeostatic
pathway involving immune cells

Target:

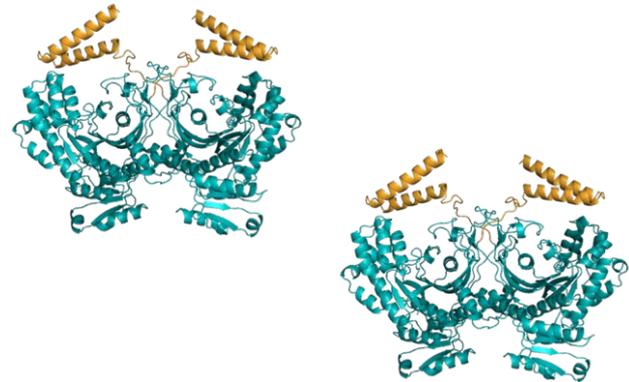
Activated T-cells via the Resokine pathway

Rationale:

Functional knockout in humans and
rodents results in increased muscle damage

Human active dosing:

3.0 mg/kg weekly or bi-weekly



Resolaris Phase 1b/2 Clinical Program: Summary of Results

Clinical Activity Signals

- Conducted three 3-month clinical trials in patients*
 - **002**: 20 adult FSHD patients
 - **003**: 8 early-onset FSHD patients
 - **004**: 10 adult LGMD2B patients and 8 adult FSHD patients
- Muscle function signals:
LGMD2B/early-onset FSHD > FSHD
- Overall patients did not feel worse as measured by quality of life questionnaire

Human Safety Profile

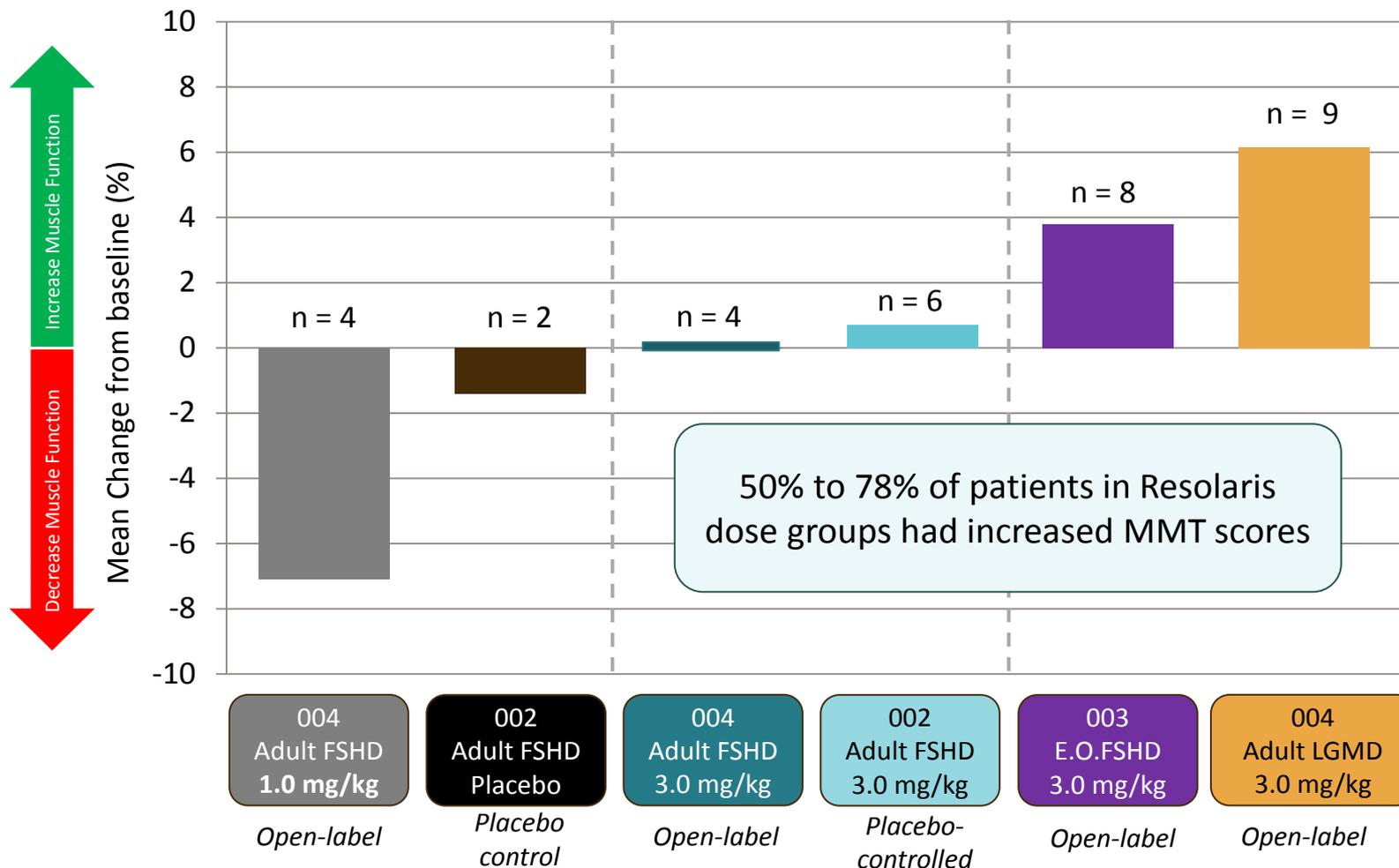
- 44 patients received Resolaris for total drug exposure of 204 patient months
- Generally well-tolerated; low-level anti-drug antibody signals did not result in clinical symptoms; some transient infusion related reactions observed
- No observed signs of general immunosuppression
- 12 patients received at least 6 months of Resolaris with no significant trends of worsening in either muscle function or quality of life assessments

Resolaris Clinical Data from Three Phase 1/2a Clinical Trials

Signals of clinical activity (improved muscle function) in patients

Overall Mean MMT Change Week 14 by Dose Group

FSHD & LGMD2B Patients From 002, 003, 004 Trials



MMT = Manual Muscle Testing a validated assessment of muscle function/strength in 14 muscle groups

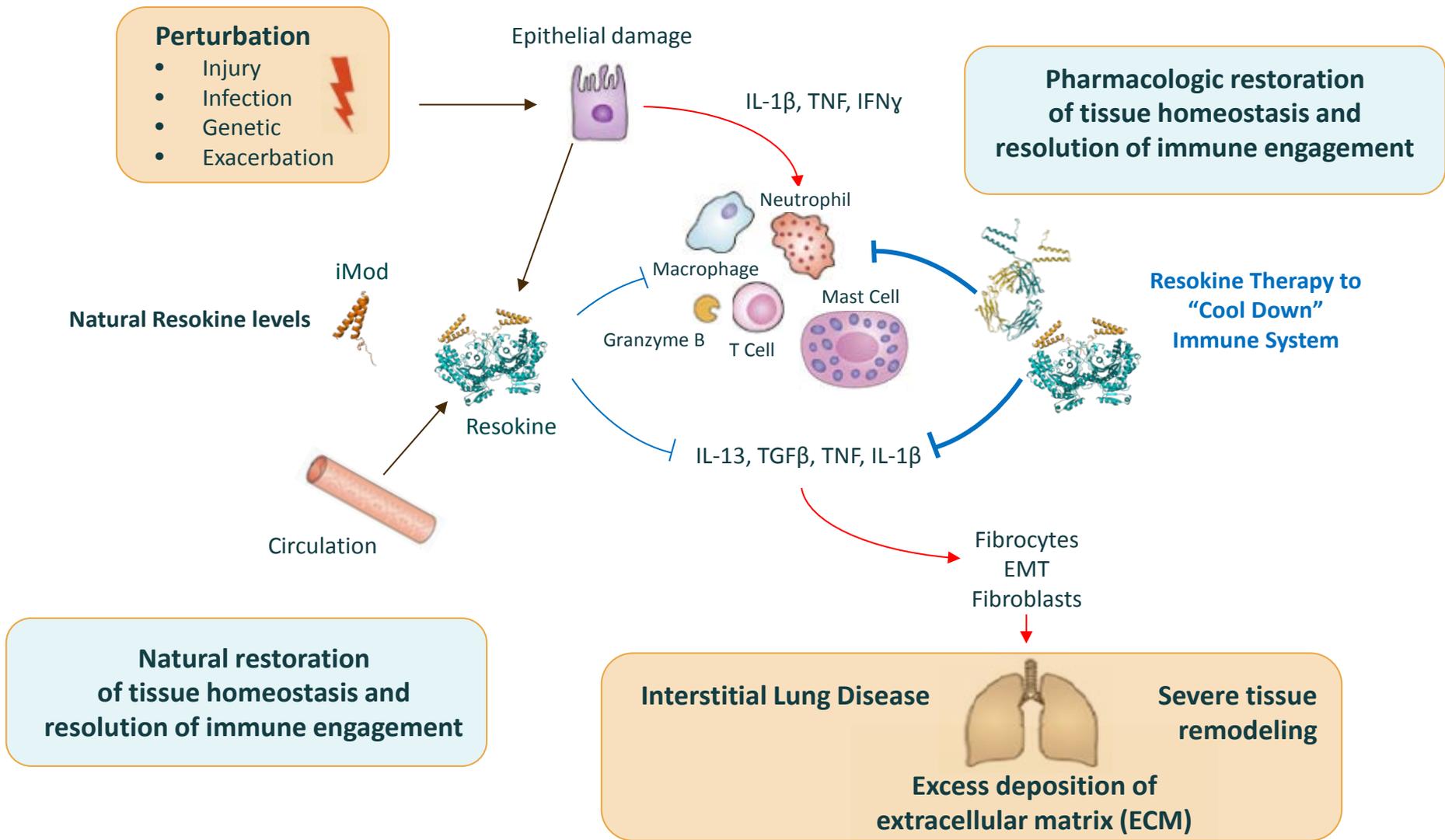
E.O. = Early Onset



IMOD.FC PROGRAM

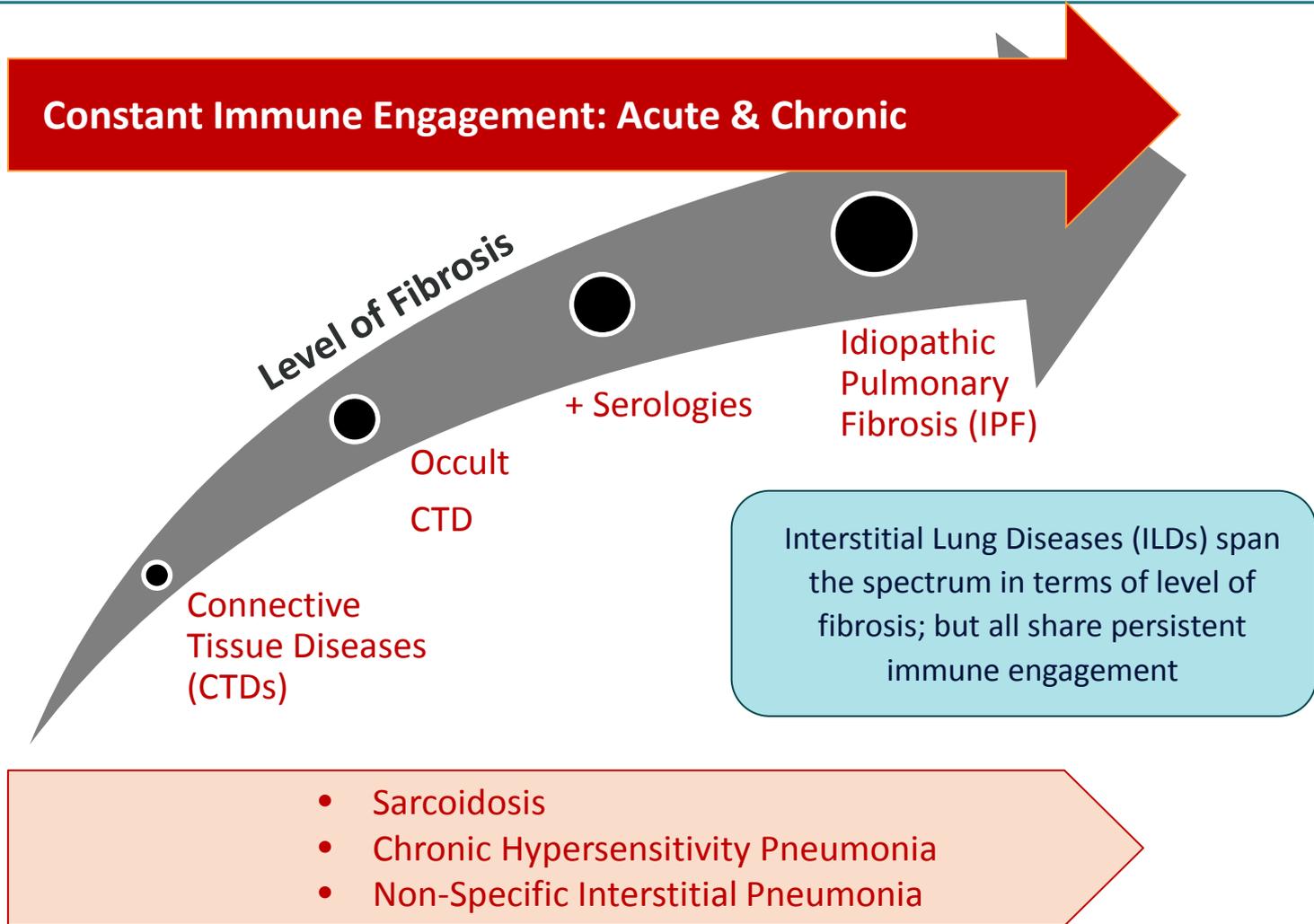
LUNG PHYSIOCRINE ENGINEERED
TO TREAT MULTIPLE PULMONARY DISEASES

Resokine Promotes Lung Homeostasis



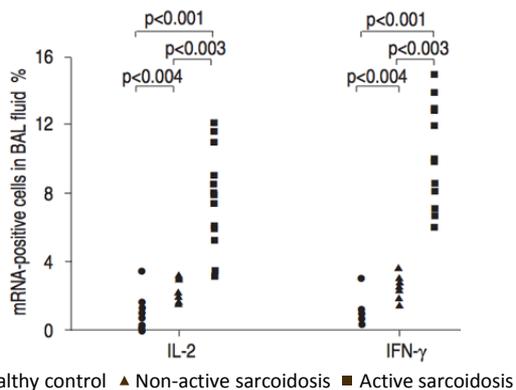
Interstitial Lung Diseases Shared Immune Engagement

Significant and persistent immune engagement provoking fibrosis



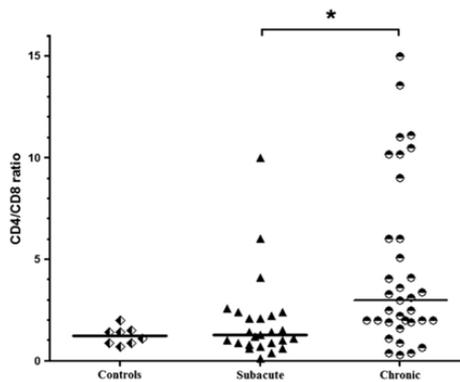
Pathophysiological Role of T Cells in ILD

Sarcoidosis

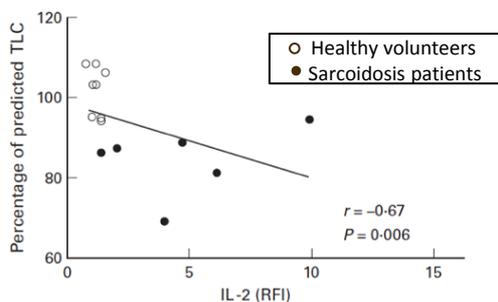
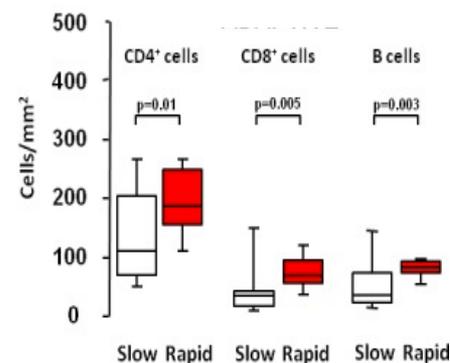


Elevated
T Cell Activity
in ILDs

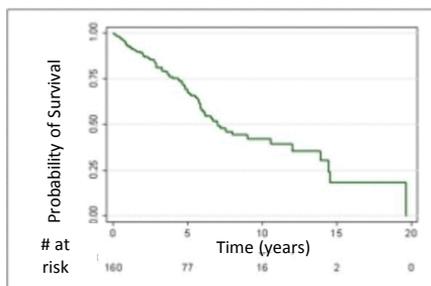
Hypersensitivity Pneumonitis



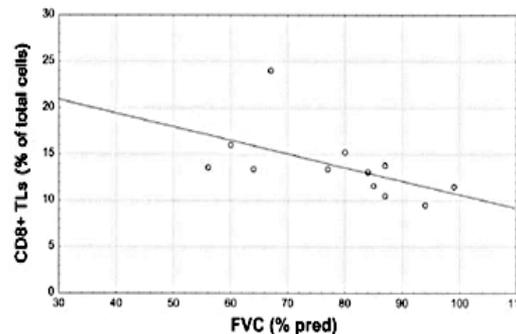
Idiopathic Pulmonary Fibrosis



T Cells
Correlated
with Negative
Outcomes



Percentage of lymphocytes in pulmonary lavage independently associated with survival



iMod.Fc Program Snapshot

Patients:

Interstitial Lung Disease (ILD) with an immune component

Therapeutic Concept:

Upregulate naturally occurring homeostatic pathway involving immune cells

Target:

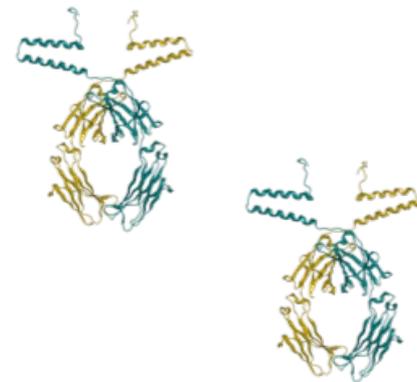
Activated T-cells via the Resokine pathway

Rationale:

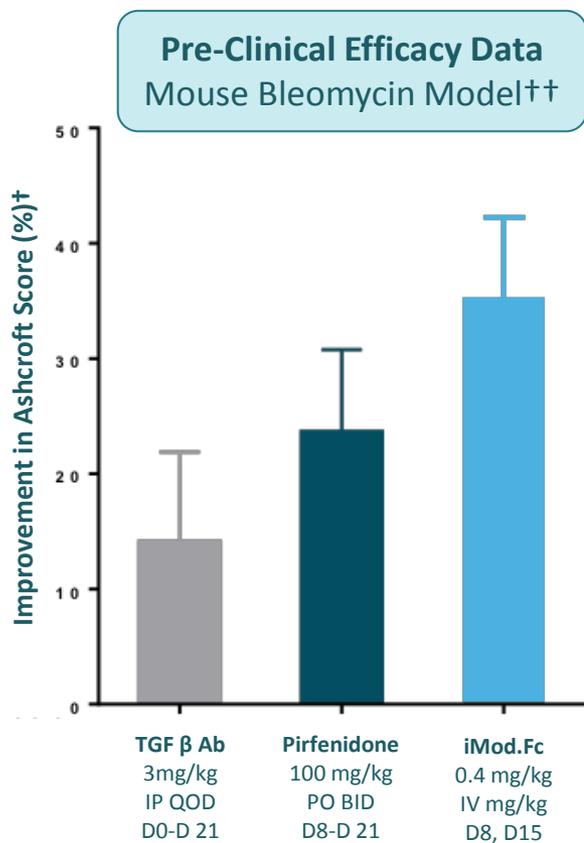
Functional knockout in humans and rodents results in lung damage

Target Administration:

Monthly dosing (IV infusion)

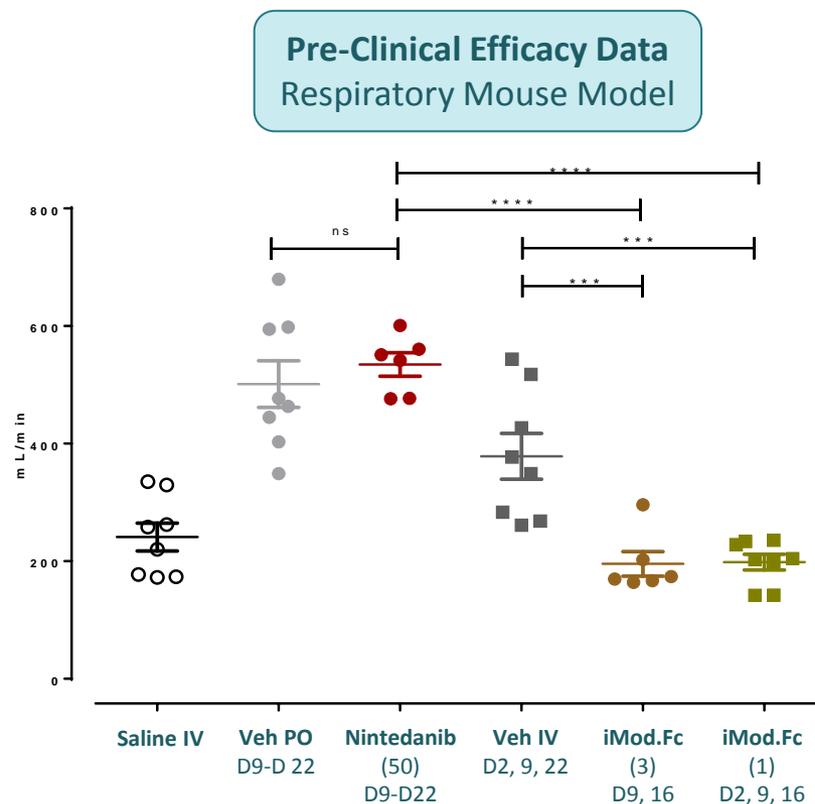


Supportive Pre-Clinical Efficacy Data



Superior activity in established IPF fibrotic model at much lower dose

† The Ashcroft scale to evaluate bleomycin-induced lung fibrosis is analysis of stained histological samples by visual assessment



iMod.Fc outperformed Nintedanib (SOC for IPF) in the respiratory mouse model at lower and less frequent dosing

*** $P \leq 0.001$; **** $P < 0.0001$; ns = not significant
Respiratory Minute Volume = amount of air inhaled/exhaled/min

Supportive Pre-Clinical Safety and PK Data

Pre-Clinical Safety Data

Non-human primate (NHP) tox

1 Month GLP tox study (also tested Rats)

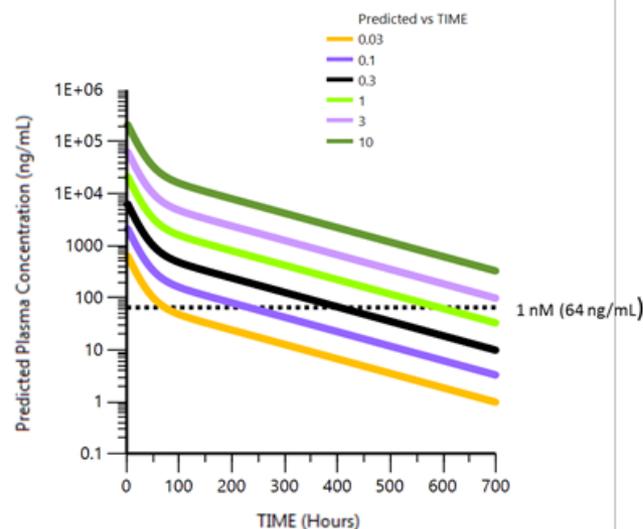
- No test article-related findings
- Weekly IV dose at 0, 10, 30 and 60 mg/kg
- NOAEL: 60mg/kg (highest tested)
- No signs of immunosuppression observed (e.g. no depression of lymphocyte counts)

3 month GLP tox study (preliminary)

- Weekly IV dose at 0, 10, 30 and 60 mg/kg
- No major clinical observations

PK

Predicted human (scaled from NHP)



$T_{1/2}$ = 4.5-7 days

(figure shows 4.5)

Safety window at planned
human doses (0.3-3mg/kg):
19-193x

First-in-Human Clinical Trials

Program Overview

(Final trial designs subject to approval)

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:

- Approximately 36 subjects
- Single study drug infusion
- Starting at 0.03 mg/kg, increasing at half-log, up to potentially 5.0 mg/kg
- Initiation – first subject expected to be dosed in the fourth quarter of 2017
- Data expected in first half of 2018

Phase 2 - Interstitial Lung Disease patients with an immune component:

- Collaborating with industry leading clinicians to develop patient trials for iMod.Fc
- First patients expected to be dosed in 2018

Market Opportunity: Potential Solution for ILD Patients in Need

Sarcoidosis

- Systemic inflammatory disorder characterized by non-caseating granulomas (CD4+ T cell driven)
- Advanced pulmonary disease is leading cause of death
- ~30% of patients have chronic inflammation, unresponsive to steroid treatment

Idiopathic Pulmonary Fibrosis (IPF)

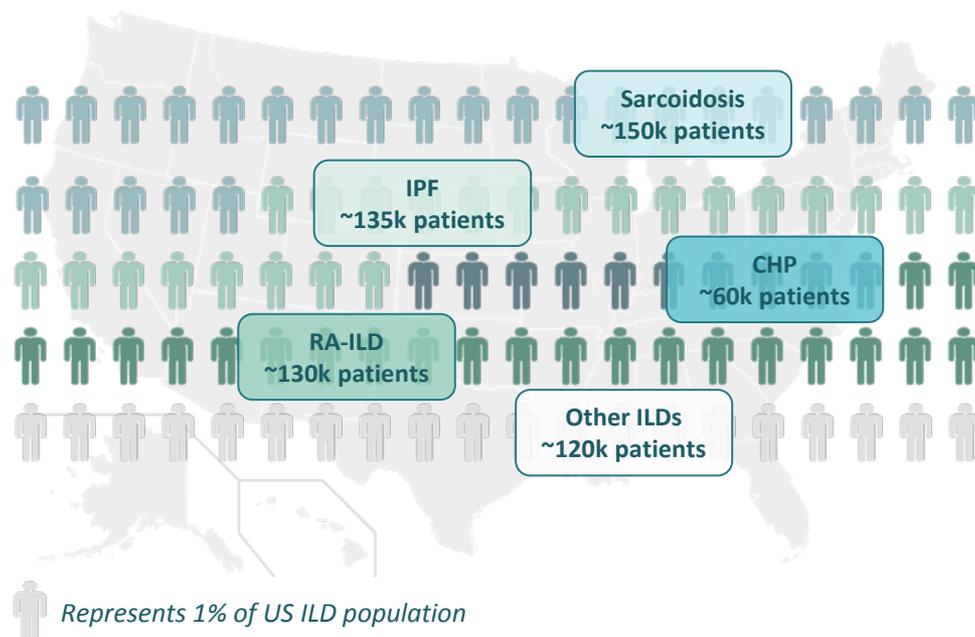
- Irreversible, progressive disease with acute episodes
- Median survival: 3-5 years
- Current SOC: Nintedanib / Pirfenidone slow functional loss but significant side effects remain (\$3B+ combined peak sales trajectory)

Chronic Hypersensitivity Pneumonitis (CHP)

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

Rheumatoid Arthritis-ILD (RA-ILD)

- Most common lung manifestation of RA: ~30% of RA patients with subclinical ILD; 10% with clinically significant disease
- Median survival: 3-10 years
- No effective therapeutic options



Other ILDs: >100 disorders

- Many secondary to other disease (e.g. Scleroderma-ILD; PM/DM-ILD)
- Various disease patterns; all with underlying inflammatory insult

Large unmet medical need

- Many have grave prognosis
- SOC has limited evidence of safety and efficacy

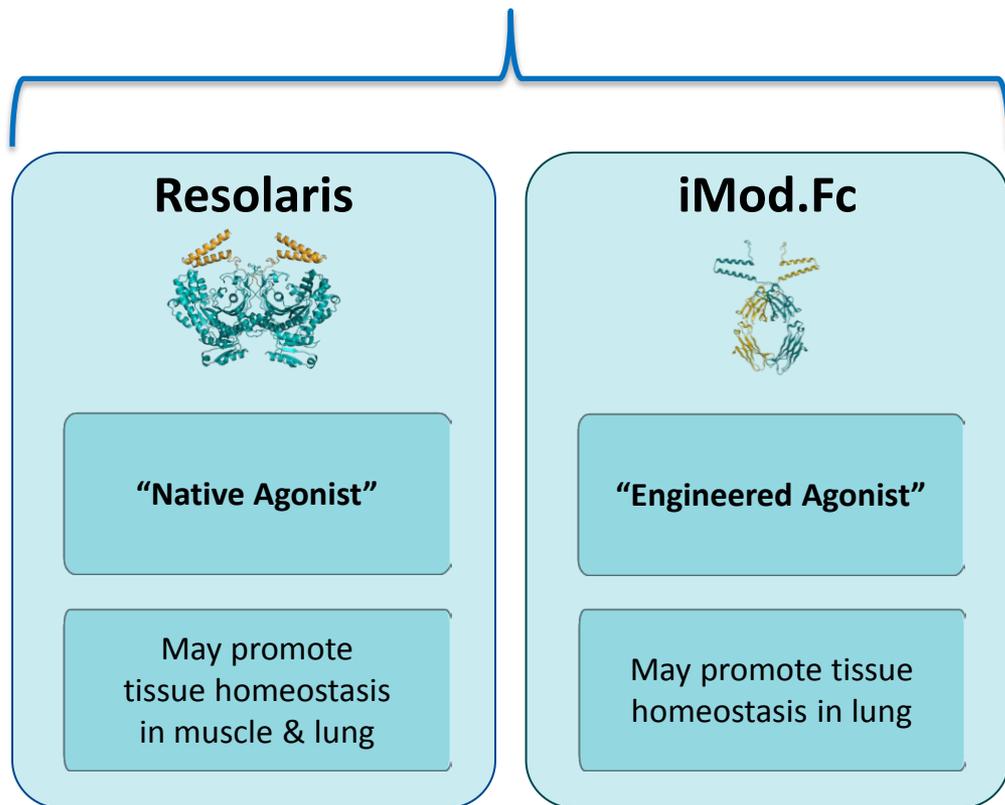


ORCA PROGRAM

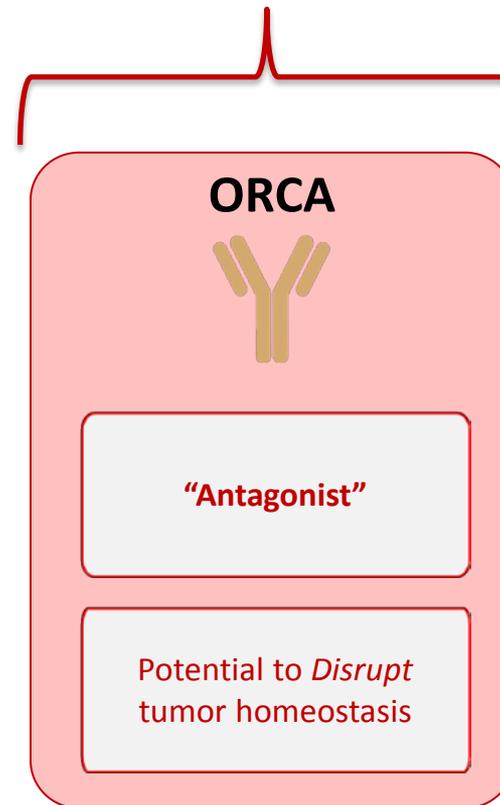
ACTIVATING T CELLS “TURNING UP THE HEAT”
TO DISRUPT TUMOR HOMEOSTASIS

ORCA Program: Activating T Cells “Turning Up the Heat” To Disrupt Tumor Homeostasis

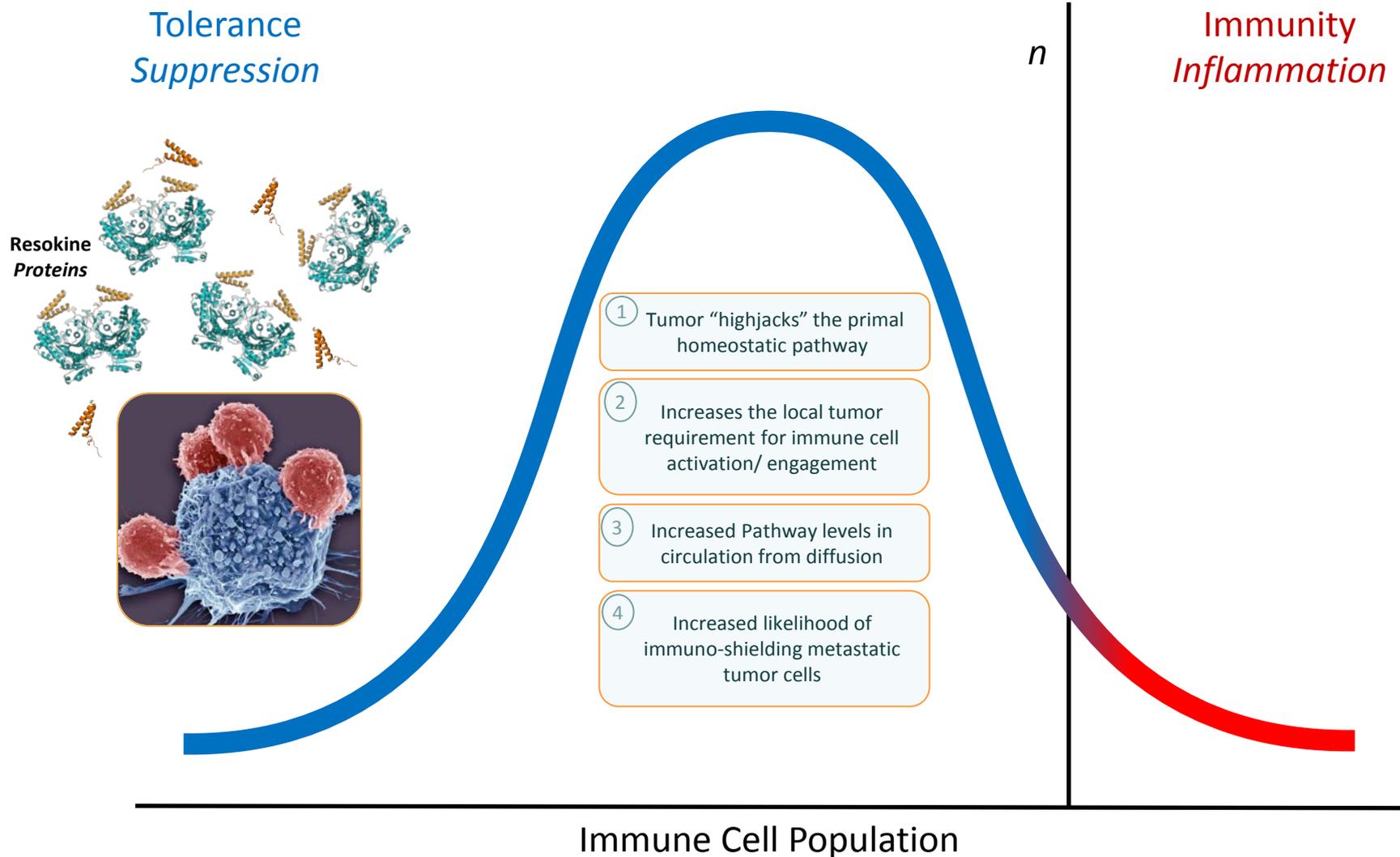
Cooling Down the Immune System



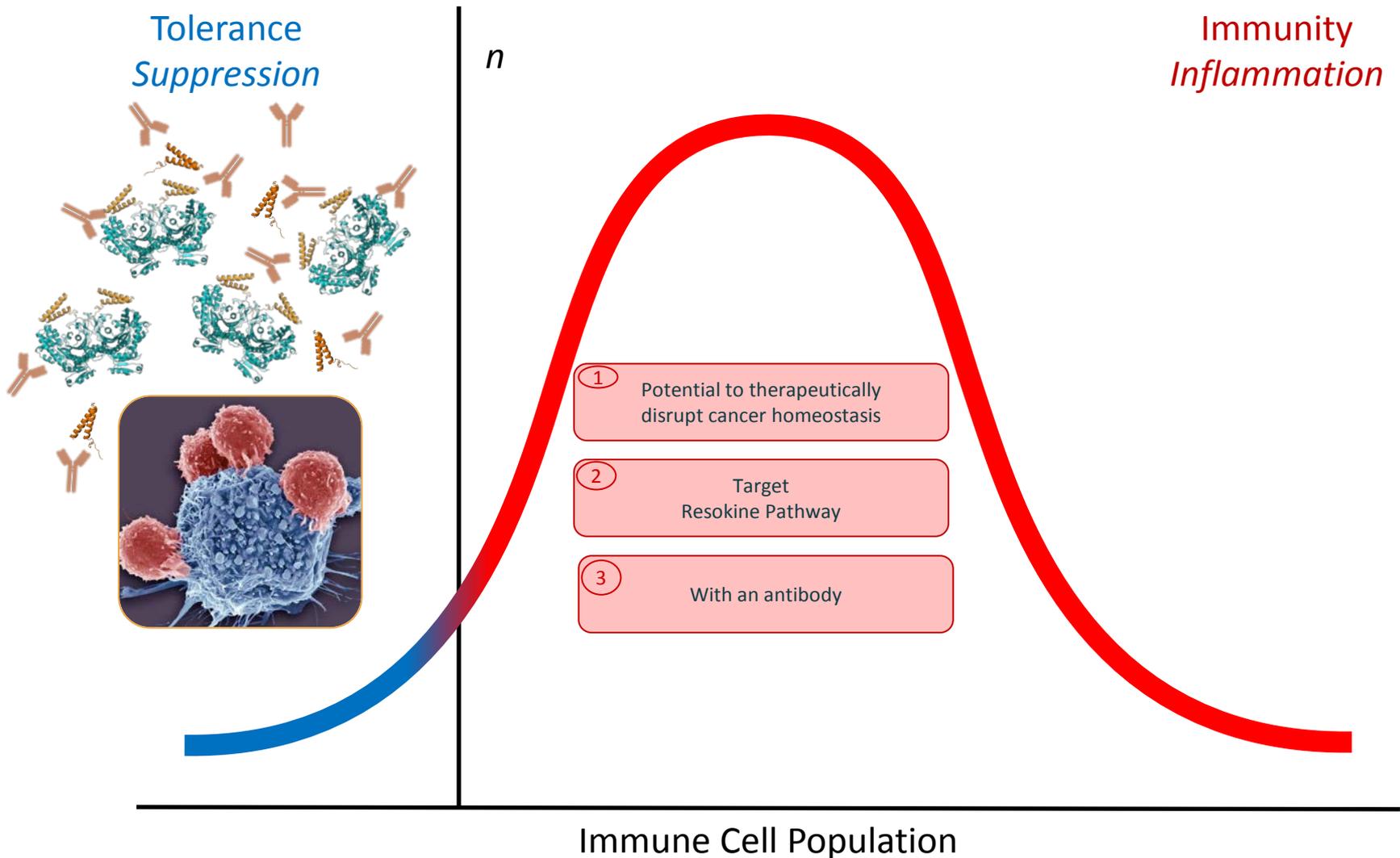
Heating Up the Immune System



Higher Resokine Levels in Tumors: Colder Immune System at the Tumor



Setting Lower Resokine Levels in Cancer Patients in Tumors: Hotter Immune System at the Tumor



ORCA Program Snapshot

Patients:

>500 patient samples in over 10 tumor types tested
~95% of patients tested positive for Resokine

Therapeutic Concept:

Resokine knockout increases T cell engagement

Target:

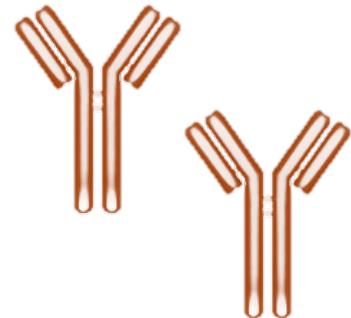
Key blocking epitope of many Resokine epitopes;
Resokine antibodies shown to knock-out pathway

Rationale:

Human evidence of antibody changing T cell behavior
(anti-synthetase syndrome patients)

Biomarker:

Liquid biopsy correlates with tumor volume and efficacy



Supportive Pre-clinical Efficacy Data

Pre-clinical Efficacy Data

Tested Resokine Abs in multiple mouse syngeneic tumor models

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

Tested Resokine Abs in combination

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

Development Timelines

Resokine antibody selection:

- On track to declare an IND candidate in fourth quarter of 2017

Scientific presentations:

- Beginning in 2018

First clinical trial in patients:

- Initiate in 2019

LIFE Leaders



John Mendlein, Ph.D.
Chief Executive Officer



Sanuj Ravindran, M.D.
Chief Business Officer



Sanjay Shukla, M.D.
Chief Medical Officer



David King, Ph.D.
SVP, Research



Grove Matsuoka
SVP, Product Programs and Planning



John Blake, CPA
SVP, Finance



Andrea Cubitt, Ph.D.
VP, Product Protection



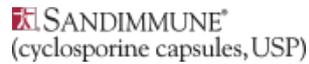
Ashraf Amanullah, Ph.D.
VP, Manufacturing



Holly D. Chrzanowski
VP, Enterprise Talent and Organization



Nancy Krueger
VP, Legal Affairs



LIFE Corporate Goals and Financial Update

Corporate Goals:

1. Advance Pipeline with Two Molecules in the Clinic

- iMod.Fc scheduled to commence Phase 1 in 2017

2. Declare 3rd IND Candidate

- ORCA program on track to declare an IND candidate in 2017

3. Partner One or More Wholly-Owned Programs

- Active discussions ongoing (Resolaris/iMod.Fc/ORCA)

Financial Update:

- \$57.2M cash and investments as of 6/30/17
- Announced Private Placement on 8/28/17 with \$45.8M in gross proceeds
- Deemed market capitalization as of closing price on 9/22/17: ~\$167M*