aTyr Pharma
NASDAQ: LIFE

Targeting Novel Immunological & Homeostatic Pathways

For Patients With Severe Immune Mediated Diseases

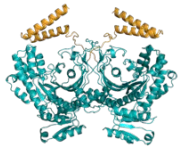
John Mendlein, Ph.D., CEO
aTyr Pharma, Inc.
Jefferies Healthcare Conference
June 9, 2017

Forward-Looking Statements

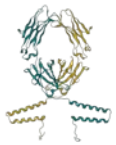
The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “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 Physiocrines and our product candidates, including Resolaris™ and our iMod.Fc 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, and 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.

LIFE Value Proposition

Pioneers of new, fundamental immunology targets
Promote Tissue Homeostasis



Resolaris in 2 rare muscular dystrophies
Favorable safety profile and potential muscle improvement



Advancing iMod.Fc, 2nd Physiocrine, program for rare lung diseases
Initiate first-in-human clinical trial 2H 2017

3rd Physiocrine-based Program in a 3rd therapeutic area
Potential 2017 IND candidate, 3rd Modality

Pursuing partnership(s) for one or more programs
to accelerate clinical and preclinical pipeline

>190 issued/allowed patents
Strong Leadership Team associated with **18** approved drugs

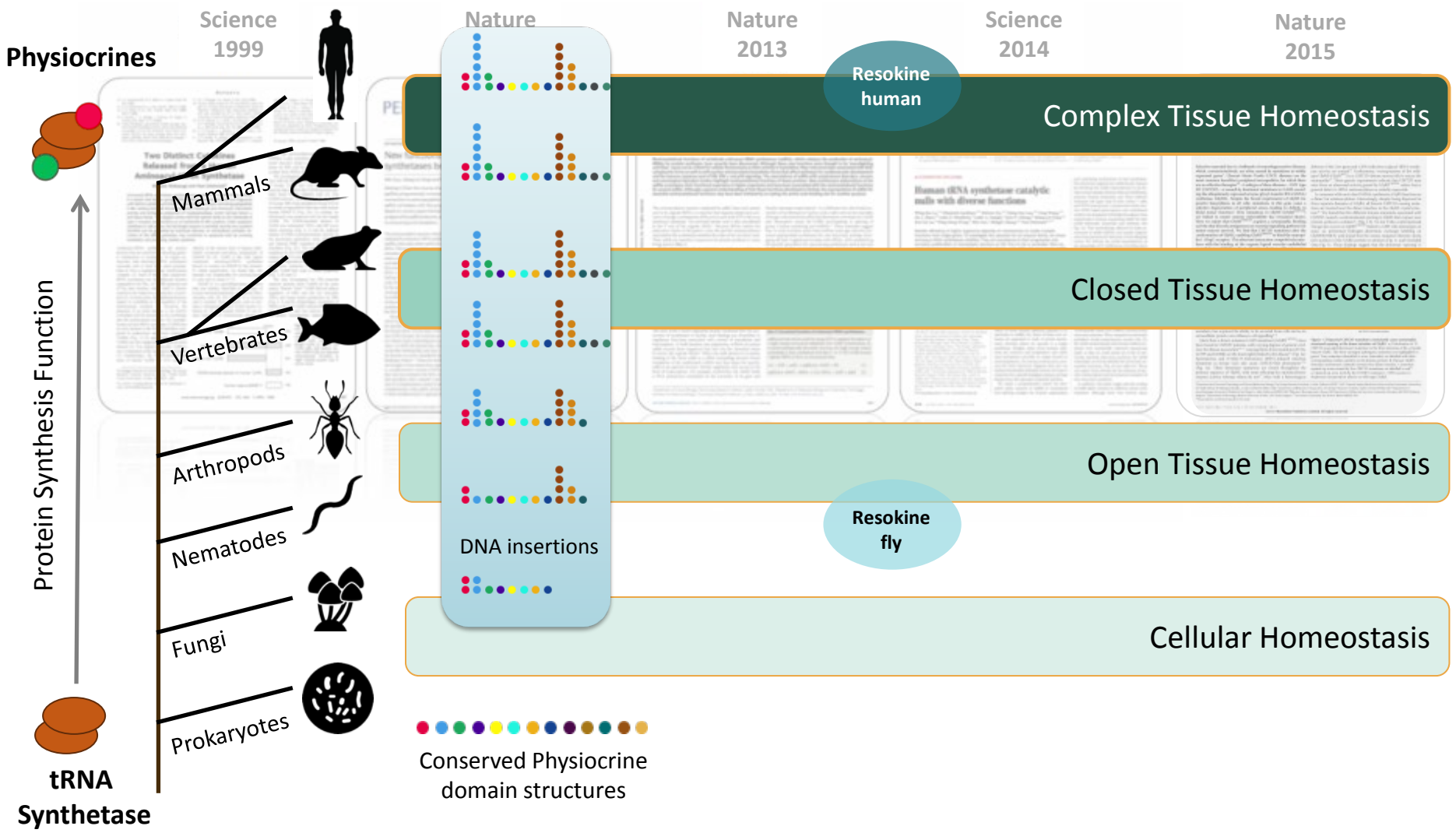
$61.9M cash and investments as of 3/31/2017
Sufficient to fund anticipated operations into **3Q 2018**

New Immunology Pathway: Resokine

Evolved from Cellular Homeostasis Genes over 400 Million Years

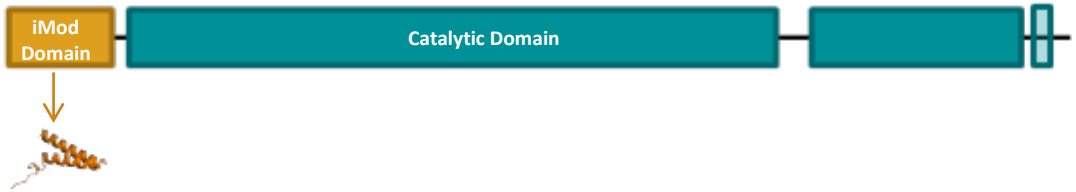
Resokine: Potential Key Regulator of Homeostasis

Evolved with system complexity



Resokine Pathway Evolved Early

Human HARS (Histidyl tRNA Synthetase)



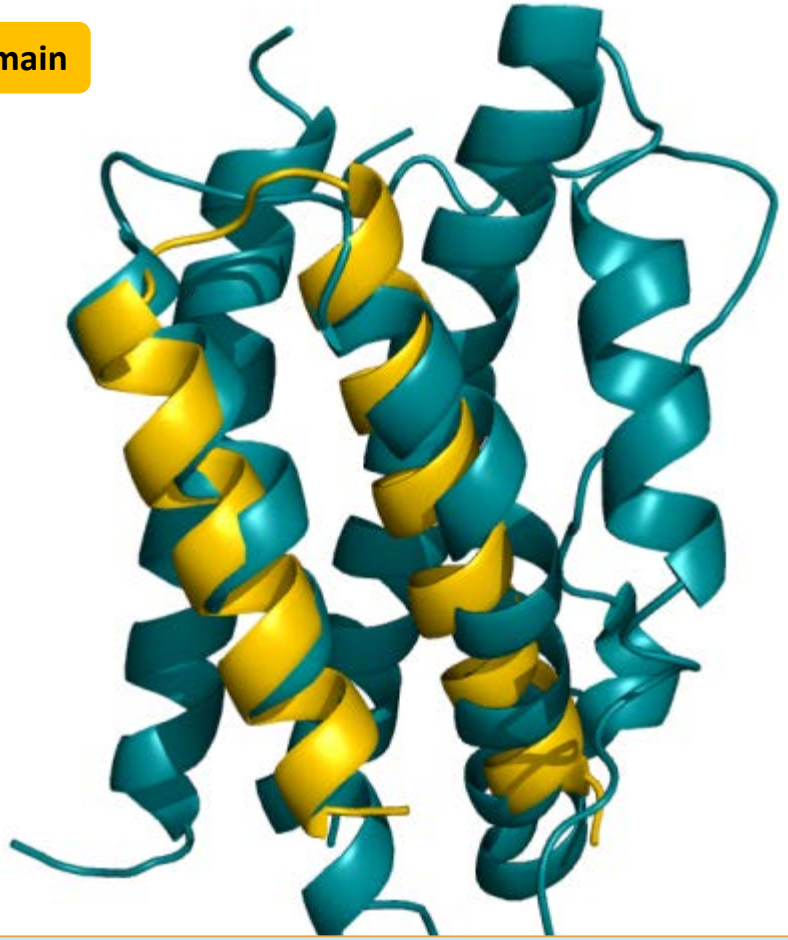
Splice variant 9: “iMod” Domain

	First evolved (~M years)	Percent identity			
		human iMod	human IL-6	human IGF-1	human Myostatin
	**1.8**	100%	100%	100%	100%
	**50**	98 %	97 %	99 %	100%
	**65**	85 %	41 %	92 %	96 %
	**265**	70 %	31 %	72 %	76 %
	**408**	50 %	-	58 %	69 %

NCBI Uniprot

Ancient, Fundamental Immune Motifs in Resokine

Resokine iMod domain

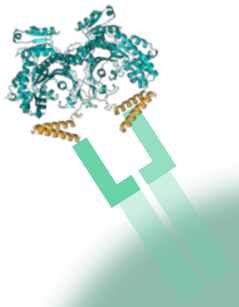


4α helical cytokine

Resokine iMod domain entered the genome of animals before IL-6 and related cytokine family

Resokine Agonists Change T Cell Phenotype

Unique MOA to orchestrate immune homeostasis in activated T cells



T cell
(activated)

Shifts trafficking & residence closer to a resting T cell

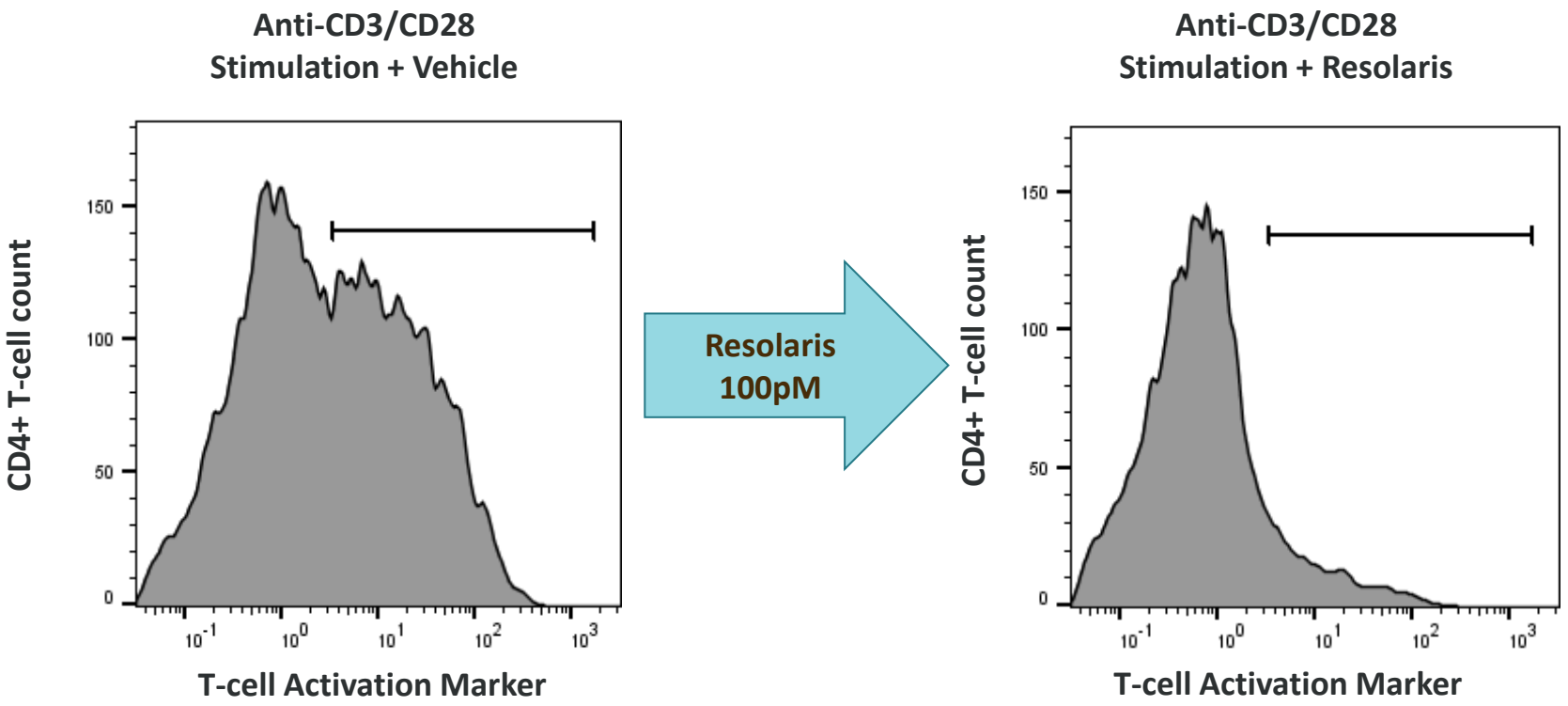
Stimulatory pathways at levels close to a resting T cell

Effector functions at levels close to a resting T cell

Without in vivo immunosuppression

Resolaris MOA: Tempers Activated T cells

Demonstrated effect as an immuno-modulator



*Resolaris with **Activated** T-cells Promotes a More **Resting** T-cell Phenotype*

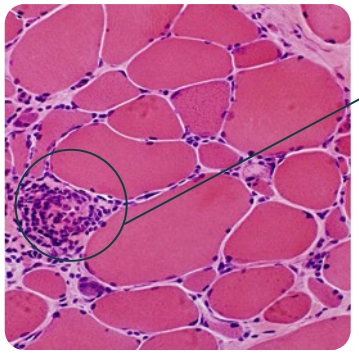
On the Left: *Gated on CD4⁺ T cells. Resolaris at 100 pM. 24 hours stimulation with anti-CD3/CD28 Abs.*

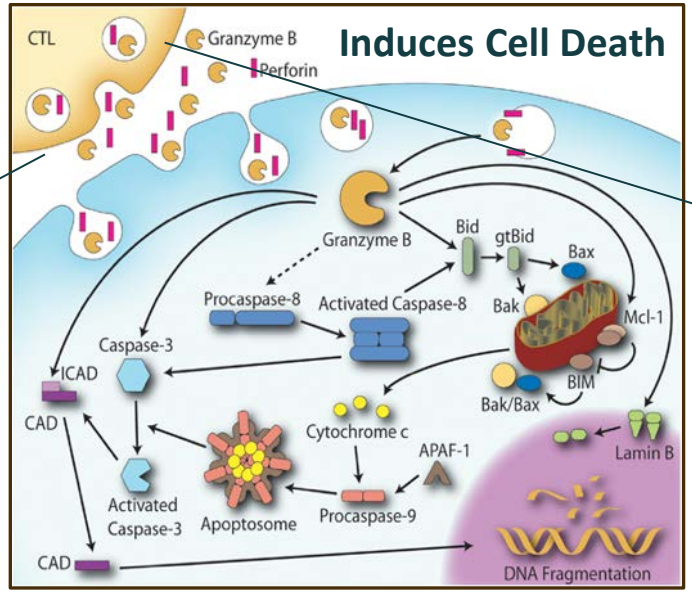
On the Right: *T cells were stimulated with anti-CD3/CD28 antibodies in the presence of vehicle or Resolaris . After 24 h, supernatants were collected and analyzed by ELISA, Statistics by T test*

How T Cells Participate in Pathology & Disruption of Homeostasis

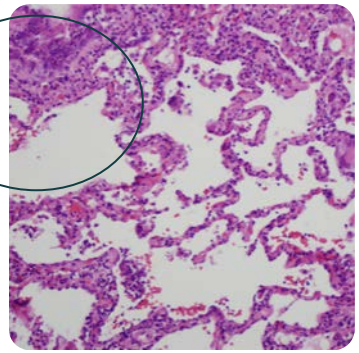
Release of Granzyme B

Muscle Disease



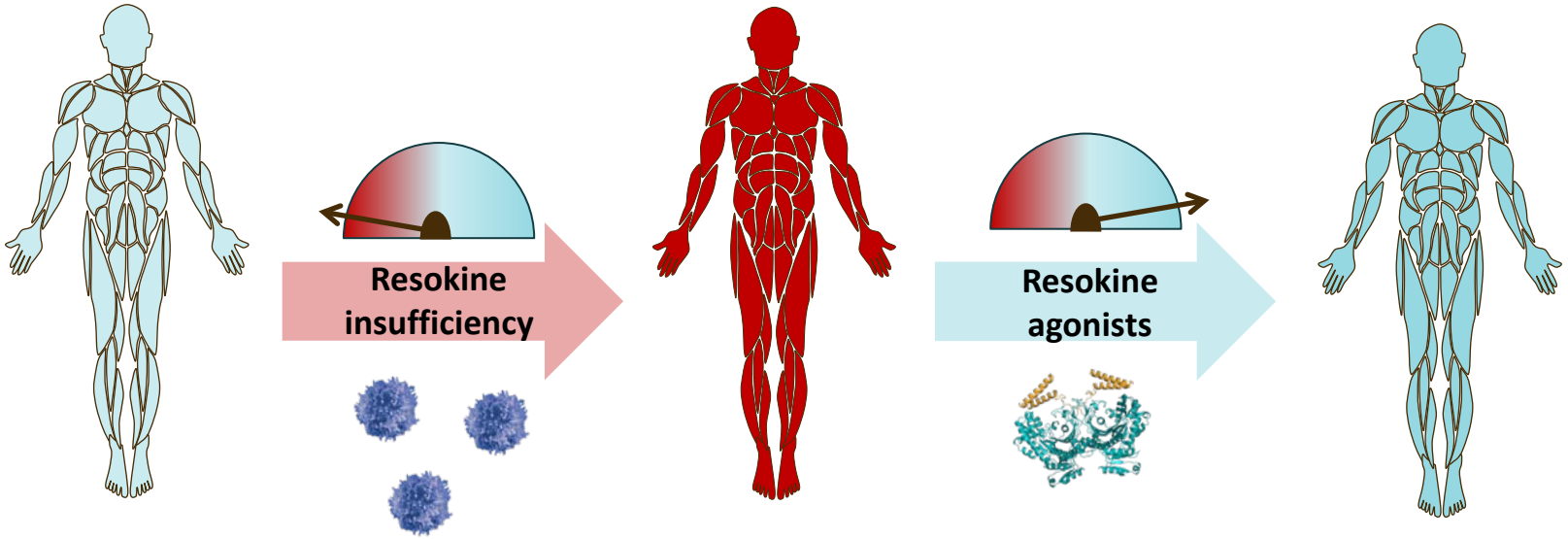


Lung Disease



Boivin et al., Lab Invest., 2009
Chen et al., Immunity, 2013

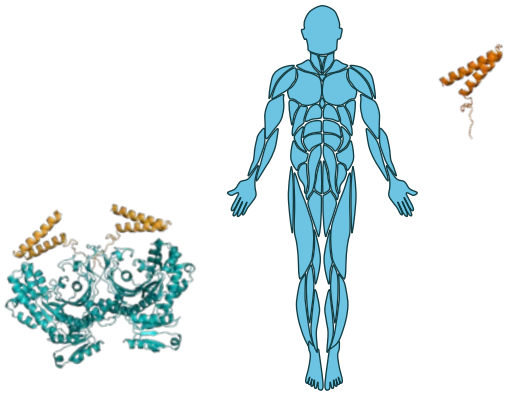
LIFE's Therapeutic Paradigm



Evidence for Homeostatic Role of Resokine in Humans

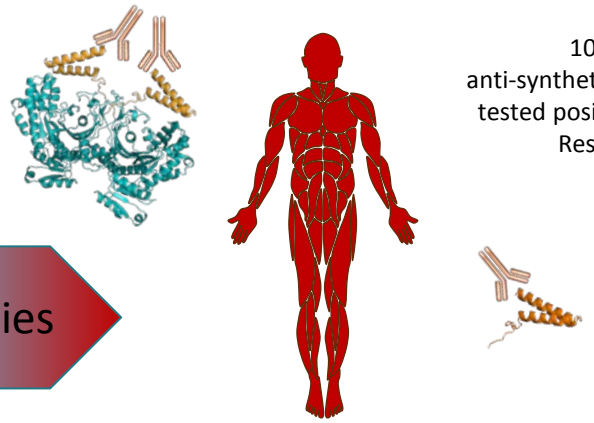
Disrupting the Resokine Pathway Promotes Muscle and Lung Disease

Homeostasis

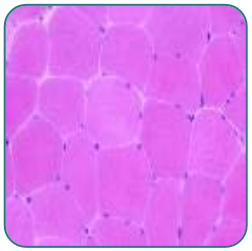


Disease-antibodies

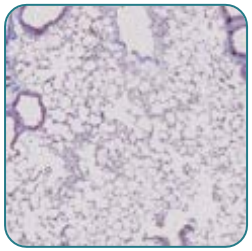
Imbalance



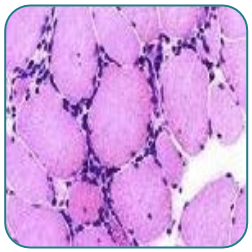
100% (18 of 18)
anti-synthetase syndrome patients
tested positive for antibodies for
Resokine proteins



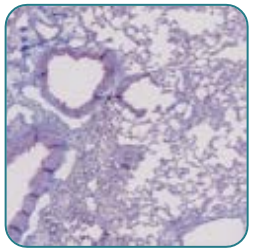
Healthy muscle



Healthy lung



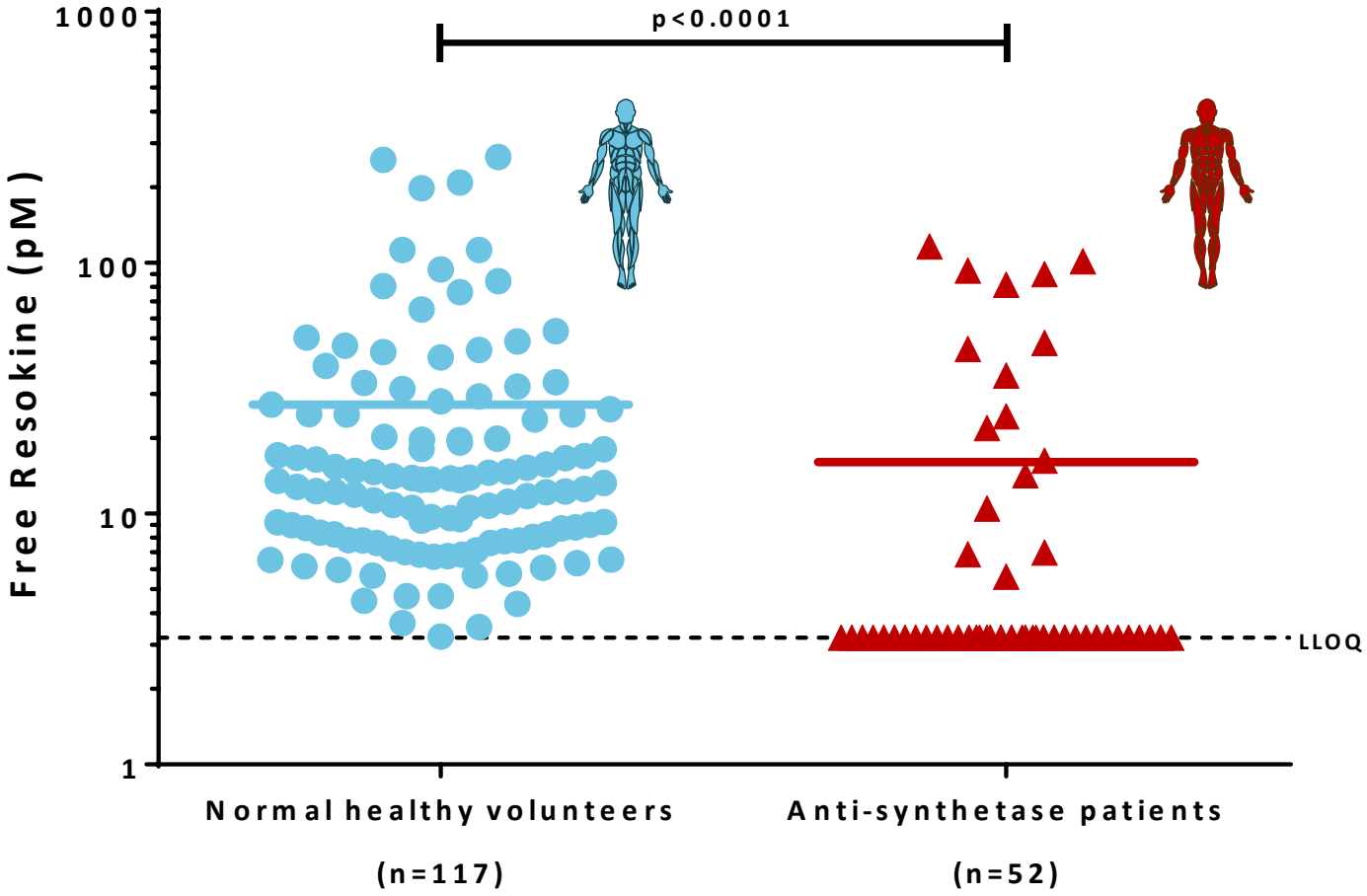
Diseased
Muscle



Diseased
Lung

↑ Immune cell invasion/activity

Free Resokine Pathway in Anti-Synthetase Patients is Diminished



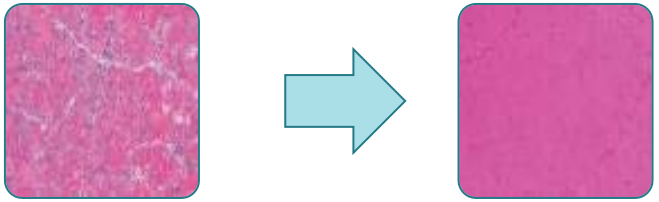
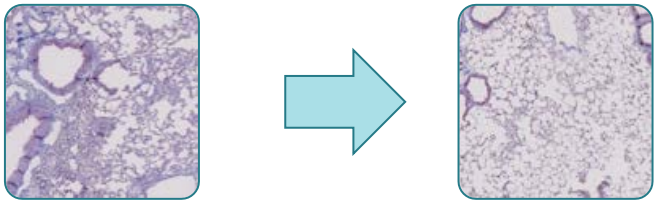
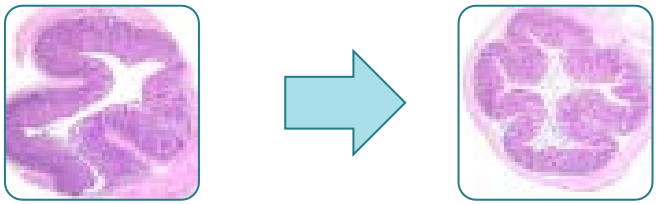
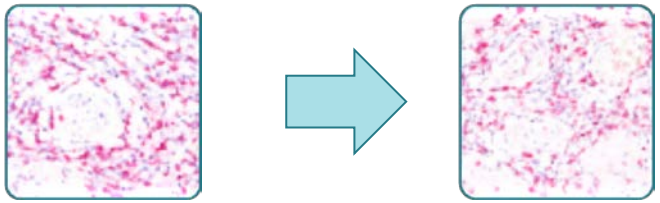
69% at or below limit of detection

Unpublished data from aTyr and collaborator

Statistics: Mann-Whitney test

Agonists of the Resokine Pathway in Immune Driven Models

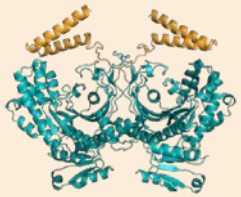
Balancing the immune response to tissue insults

Disease Model	Resokine Homeostatic Effect	Immune Targets
Skeletal Muscle Statin Induced Myopathy		CD4/CD8 & macrophages
Lung Bleomycin Induced Lung Fibrosis		Th17/CD4
Colon TNBS Induced Colitis		Th17/CD4
Skin IL23 Induced Psoriasis		Th17/CD4

In vivo administration of Resokine proteins to animal models of T cell driven disease states.
Cell type indicates type of cells involved but may not be limited to these cells.

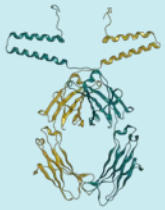
Three Therapeutic Areas, Three Therapeutic Modalities Harnessing New Immunological Insights

Resolaris



- "Native Approach" to agonize Resokine pathway
- Muscle homeostasis
- No observed signs of immunosuppression
  Signals of potential improved muscle function
- Rare muscular dystrophies

iMod.Fc



- "Engineered Agonist"
  Splice variant of Resokine pathway fused to Fc of antibody
- Lung homeostasis
- Functional knockout disrupts lung homeostasis
  IPF rodent model data compared to Pirfenidone & Nintedanib
- Interstitial lung disease

ORCA

- 3rd Modality
- Tissue homeostasis
- Preclinical activity
- Pan therapeutic area potential

***IPF** = Idiopathic Pulmonary Fibrosis*

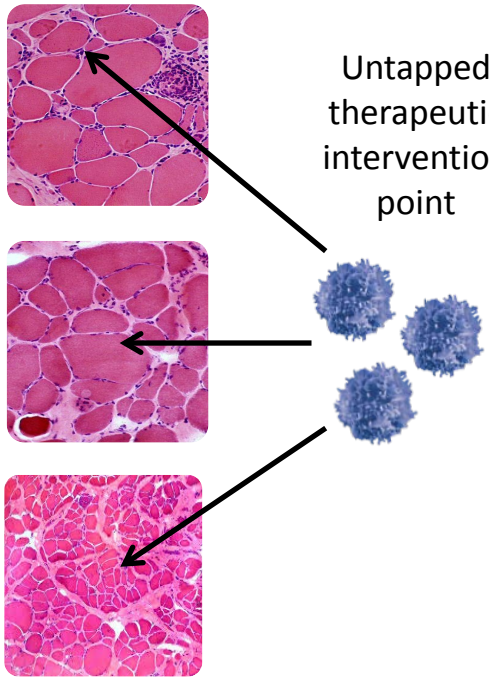
Resolaris Program

Harnessing the Resokine Pathway to Treat Multiple Rare Muscle Diseases

Rare Myopathies with an Immune Component

Chronic damage, homeostasis disrupted

Genetic Mutation	Aberrant Protein Expression	Localized T Cell Invasion/Engagement
FSHD	Inappropriate Proteins in muscle	
LGMD2B	Mutated Dysferlin proteins in muscle	
DMD	Mutated Dystrophin proteins in muscle	



Potential to link genotype to specific T cell phenotype
All debilitating diseases with little or no therapeutic treatments

Frisullo et al., J. Clin. Immunol., 2011. Gallardo et al. Neurology, 2001. Flanigan et al. Human Gene Therapy, 2013.

***FSHD** = Facioscapulohumeral Muscular Dystrophy. **LGMD2B** = Limb Girdle Muscular Dystrophy 2B.*
***DMD** = Duchenne Muscular Dystrophy.*

Resolaris in Adult LGMD, Adult FSHD & Early Onset FSHD

Evaluate Safety and Tolerability

- ✓ Build safety dossier
- ✓ Across doses
- ✓ Different patients

Evaluate Potential Activity Assessments*

- ✓ Functional / Strength: MMT
- ✓ Patient Reported Outcomes: INQoL
- ± MRI / Biomarkers assessment

Trial	Patients	Highest Dose	Design
002	Adult FSHD (n=20), ages 18-70	3.0 mg/kg Weekly (12 weeks)	Placebo controlled, Double blinded
003	Early onset FSHD (n=8), ages 16-20	3.0 mg/kg Weekly (6 weeks)	Open-label, Intra-patient Dose Escalation for 12 weeks
004	Adult LGMD2B (n=10), ages 18-70 Adult FSHD (n=8), ages 18-70	3.0 mg/kg Biweekly (4 weeks)	Open-label, Intrapatient Dose Escalation for 12 weeks

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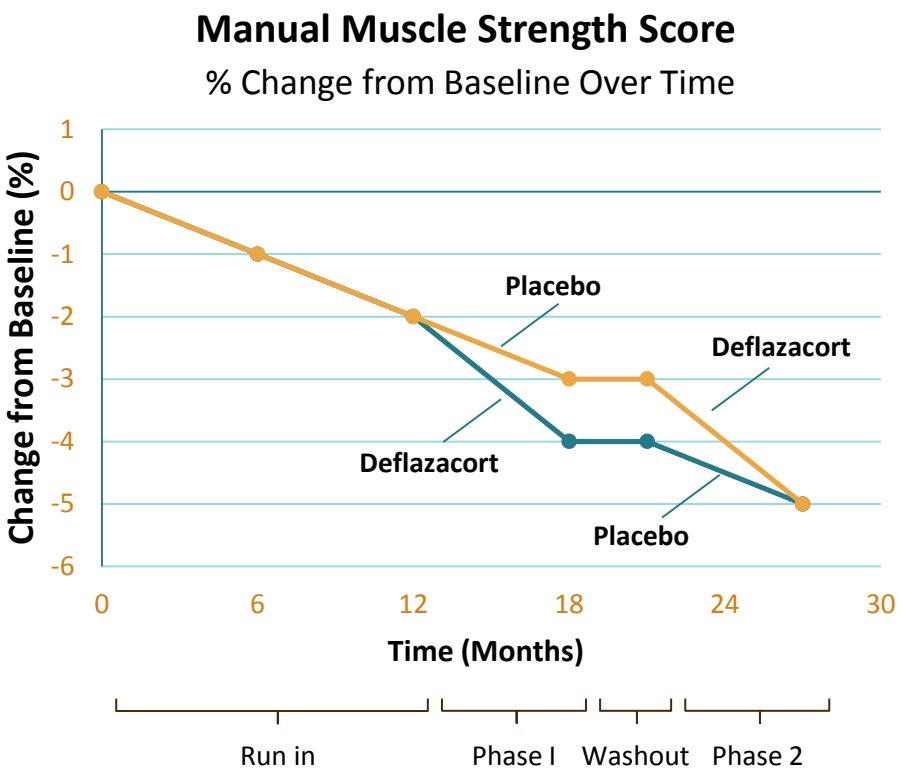
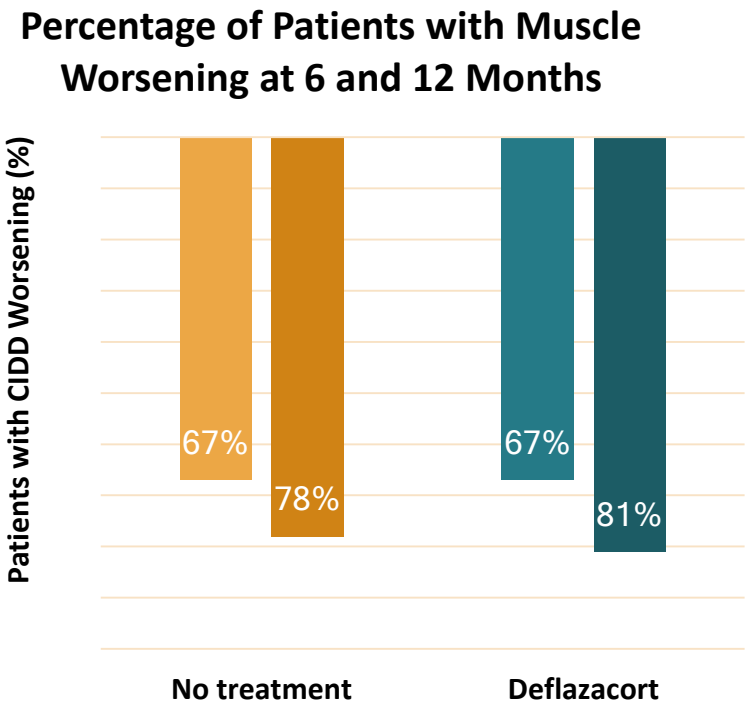
**MMT = Manual Muscle Testing, a validated assessment tool that measures muscle function/strength*

INQoL = Individualized Neuromuscular Quality of Life, a patient reported outcome measure designed specifically for neuromuscular disease

LGMD2B Patients Manual Muscle Strength Progressively Declines





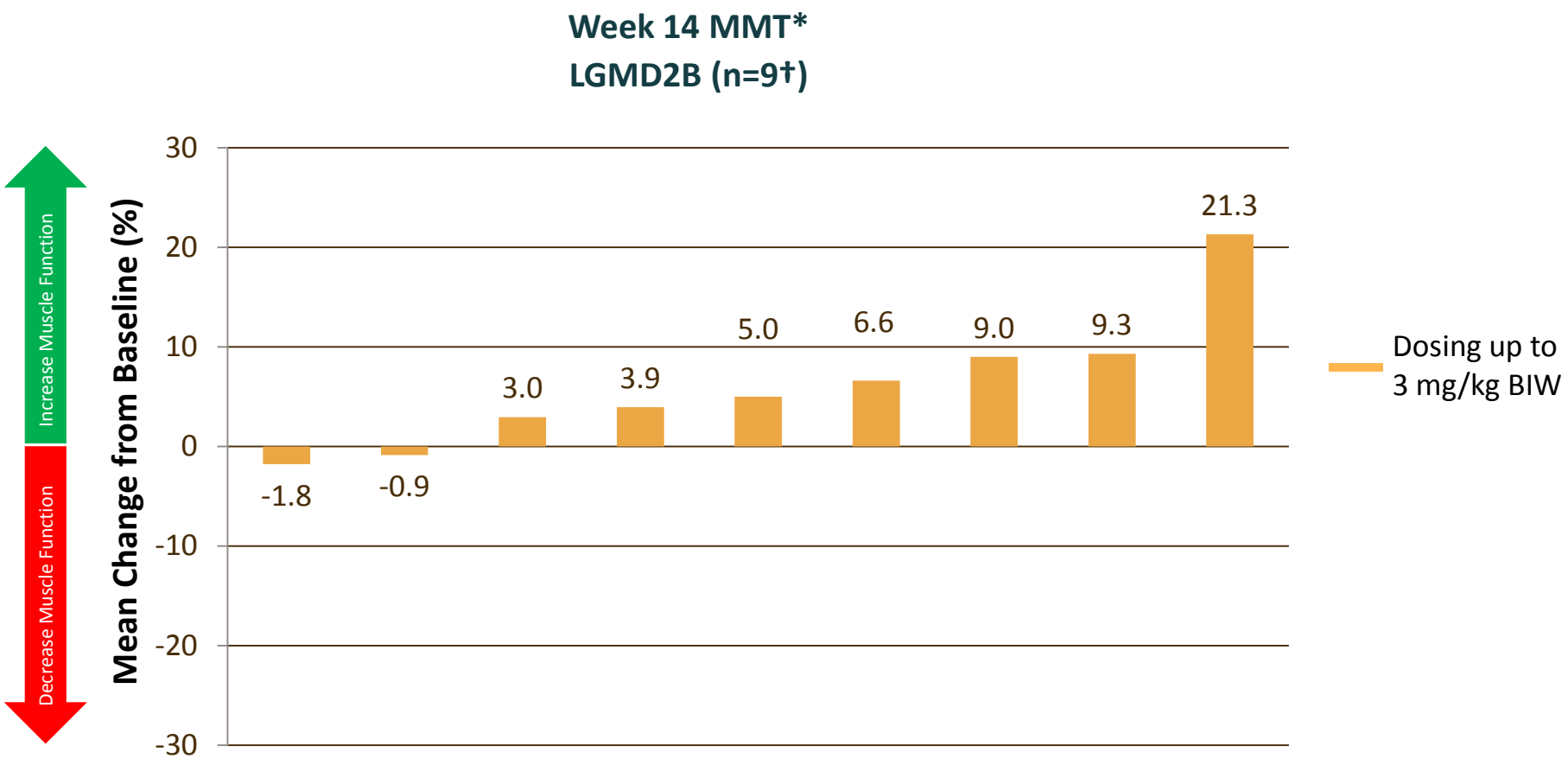
Treatment with Deflazacort was for 6 months in each arm. Single site, placebo controlled, cross over design (n=25)

Manual muscle strength assessed bilaterally by the modified Medical Research Council Scales (MRC)
CIDD (Clinical Investigation of Duchenne Dystrophy) score, graded from 0 (worst) to 10 (best)

Walter et al, Orphanet Journal of Rare Diseases, 2013

Manual Muscle Test (MMT) Scores LGMD2B Patients

004 Study: Individual Patient Changes from Baseline (%)

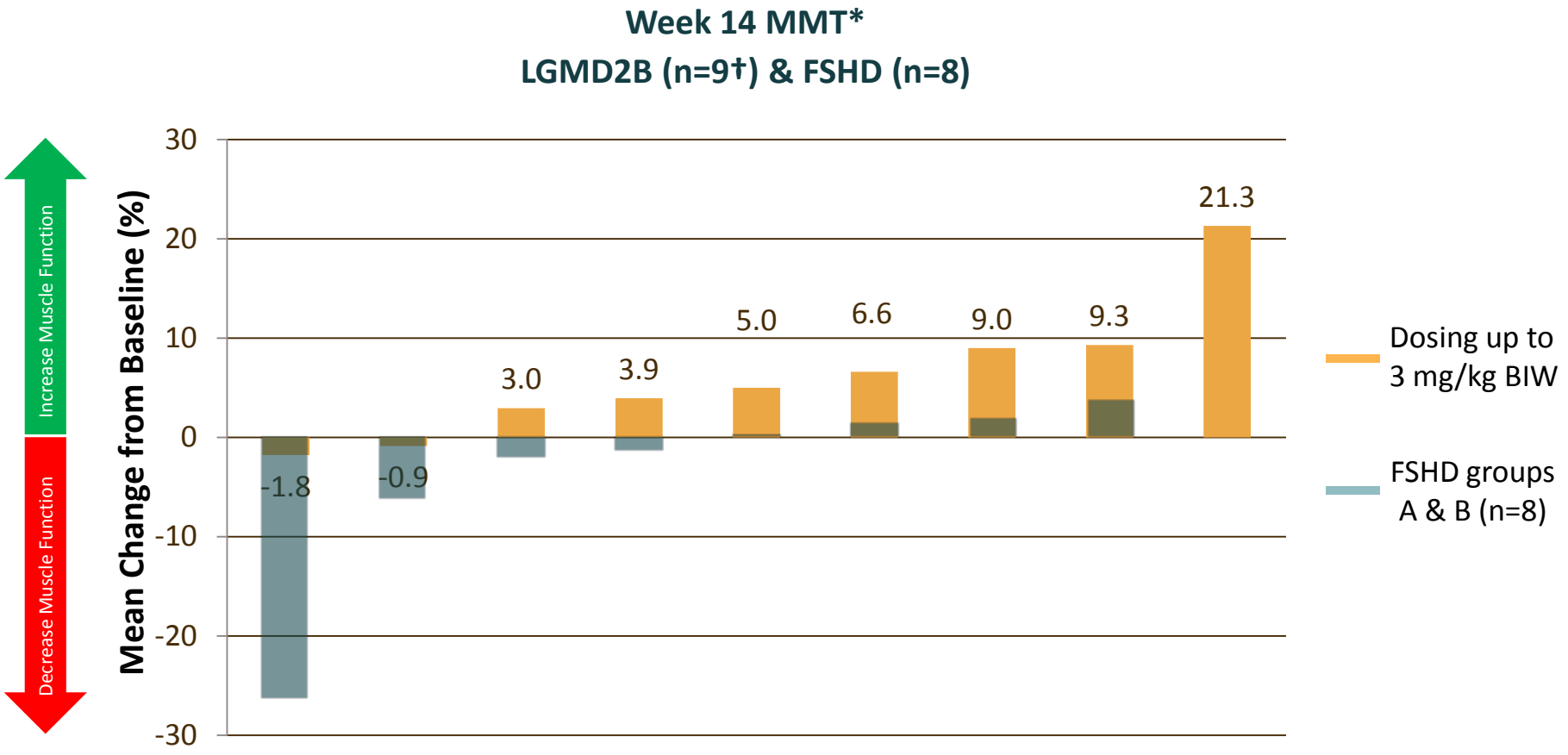


**1-week follow-up is earlier than week 14 for 2 early discontinuations; Manual Muscle Testing (MMT) a validated assessment of muscle function/strength in 14 muscle groups*

† One patient in 004 Trial did not have an MMT measurement due to being wheelchair bound at baseline

Manual Muscle Test (MMT) Scores LGMD2B & FSHD Patients

004 Study: Individual Patient Changes from Baseline (%)



**1-week follow-up is earlier than week 14 for 2 early discontinuations; Manual Muscle Testing (MMT) a validated assessment of muscle function/strength in 14 muscle groups*

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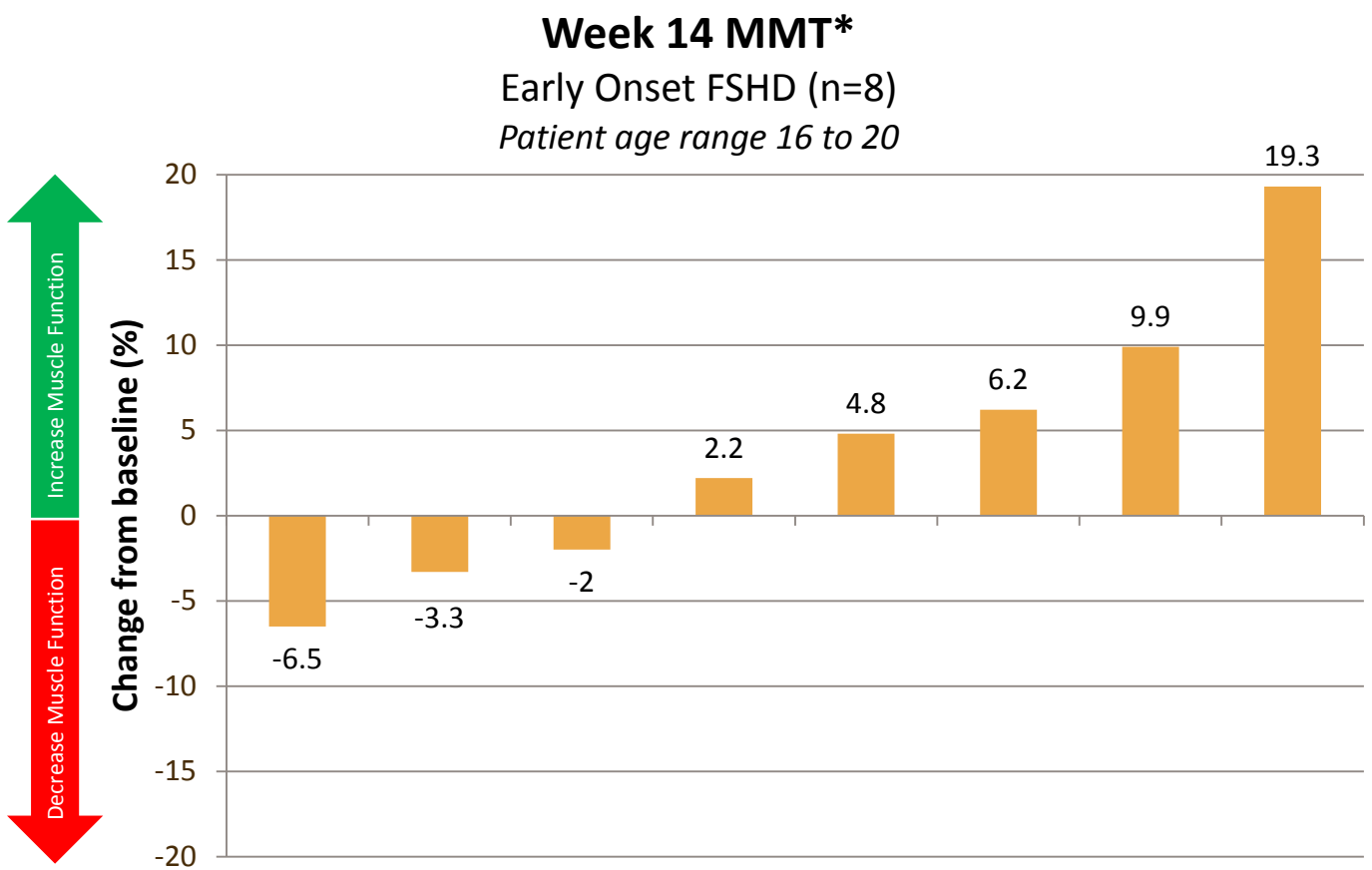
MMT Scores Early Onset FSHD Patients

Individual Patient Changes from Baseline (%)



Note: Patient with 2.2% improved from baseline originally was reported as 1% change in December interim analysis and was corrected for this presentation.

**Manual Muscle Testing (MMT) a validated assessment of muscle function/strength in 14 muscle groups*

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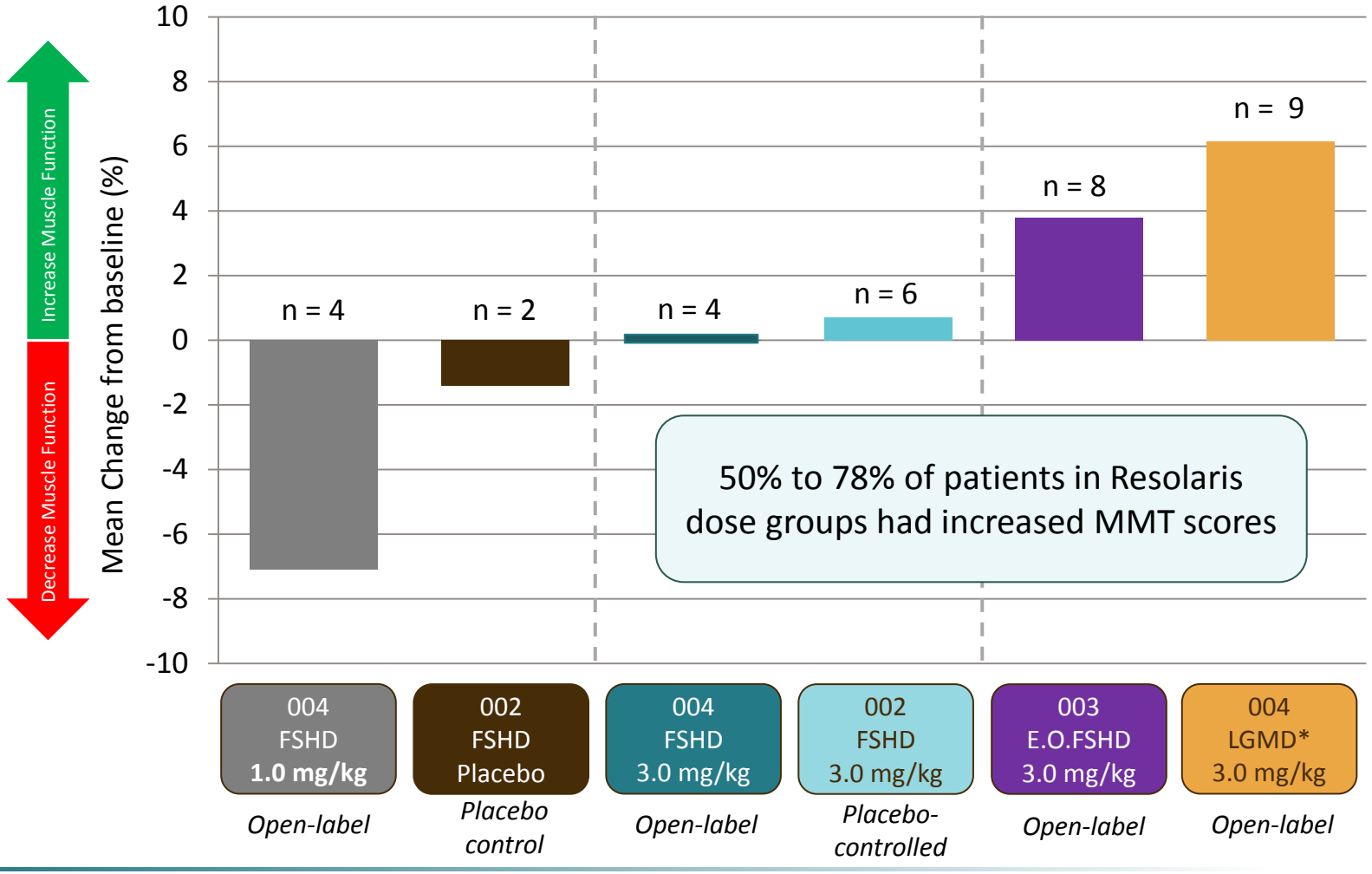
Compiled Data from Three Phase 1b/2 Clinical Trials

Relatively Stable or Improved Muscle Function Observed

Overall Mean MMT* Change Week 14 by Dose Group

FSHD & LGMD2B Patients From 002, 003, 004 Trials



** Manual Muscle Testing (MMT) a validated assessment of muscle function/strength in 14 muscle groups*

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Robust Safety & Tolerability Dossier

*44 patients have received Resolaris for a total drug exposure of 149 patient months**

No observed signs of general immunosuppression

Consistent with a homeostatic pathway working at a tissue level

Generally well-tolerated across all doses tested
Multiple myopathies; various age-groups; long-term exposure
No serious adverse events reported by investigators

Low-level anti-drug antibody assay signals did not result in clinical symptoms
Protocol discontinuations primarily driven by transient infusion related reactions

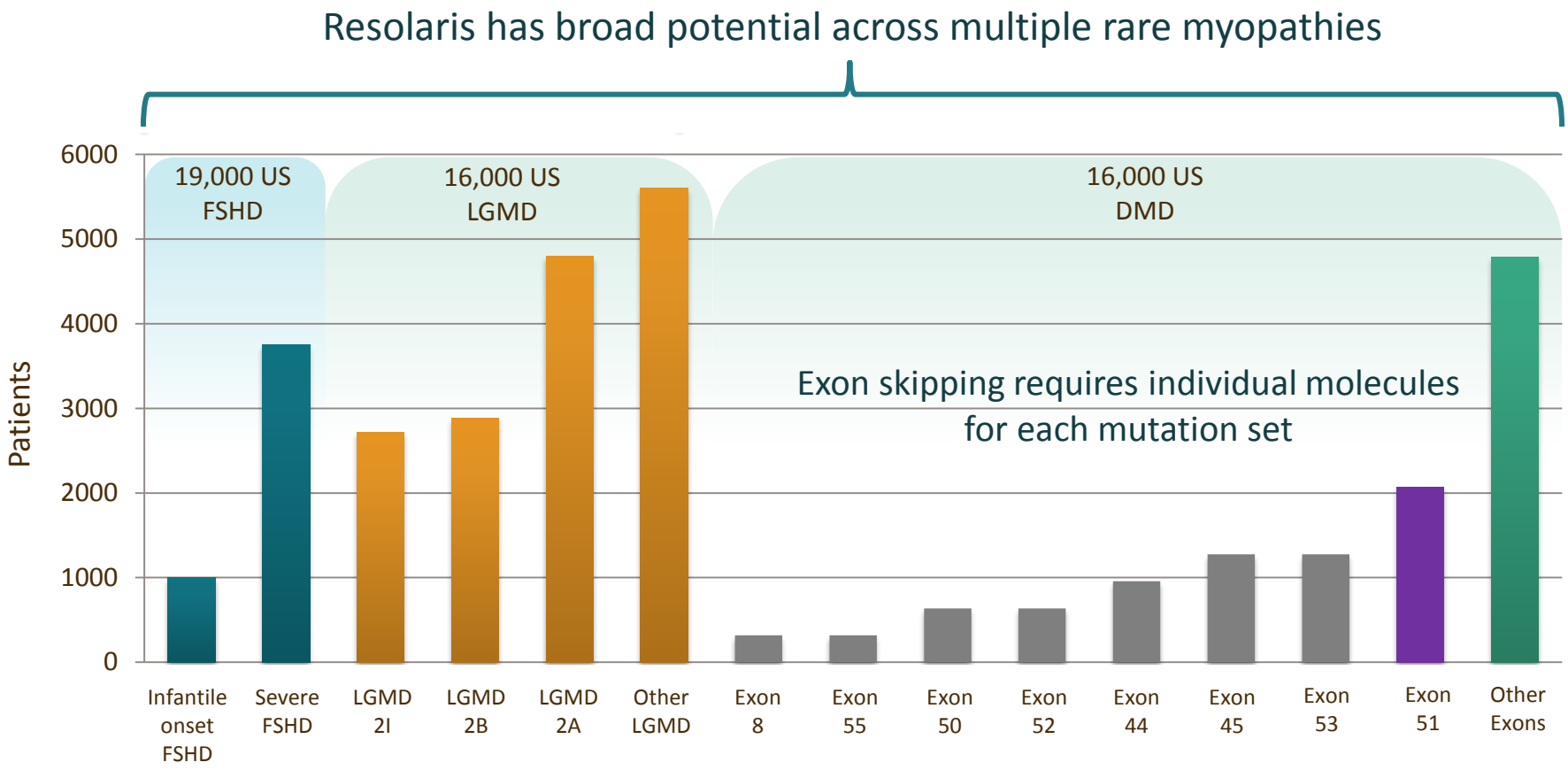
Target Product Profile (Discontinuation Rate ≤ 10%)

- *Potential to pre-medicate patients*
- *Potentially relax cut-off criteria for discontinuations*

**as of December 2016*

Resolaris: One Product, Multiple RMICs

Promise for severely afflicted myopathy patients



***FSHD**: Average prevalence rates of FSHD are approximately 1/17,000. Applying this rate to the US population based on recent census data equals approximately 19,000.*
***LGMD:** 16,000 cases estimated in US population. 1/20,000 Wickland and Kissel, Neural. Clin. 20`14. Relative Prevalence of Limb Girdle Muscular Dystrophies in the United States Population. Wicklund et al., Neurology 2013.*
***DMD:** Prevalence of approximately 5/100,000. Orphanet Report Series - Prevalence of rare diseases: Bibliographic data - May 2014 - Number 1*

Resolaris Status and 2017 Development Goals

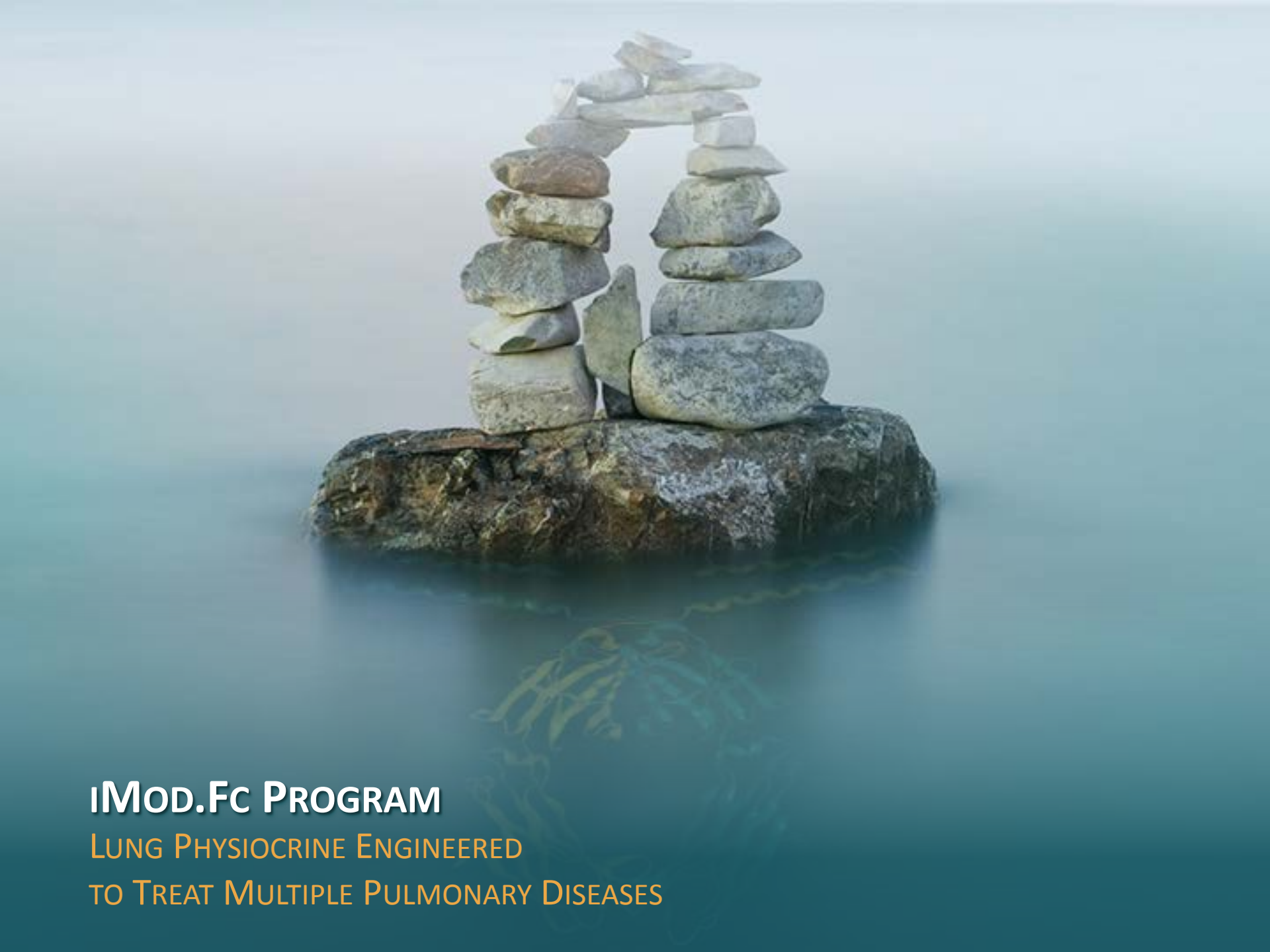
Milestones

- ✓ Muscle Function Signals: Adult LGMD2B; Early onset FSHD > Adult FSHD
- ✓ Established a favorable safety profile and identified an active dose
- ✓ Commercial scale manufacturing to be ready for future larger randomized controlled trials
- ✓ Fast Track designations for Resolaris to treat FSHD and LGMD2B

2017 Development Goals

- ✓ **Clinical Results:** Early Onset FSHD Patient Trial (003)
- **MOA:** Introduce Mechanistic/PD Assay
- **Clinical Trial:** Kick off next randomized controlled trial post partnership*

*Partner for one or more programs

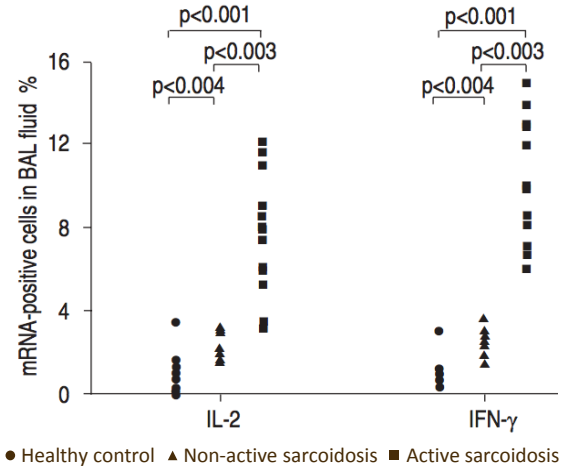


iMod.Fc Program

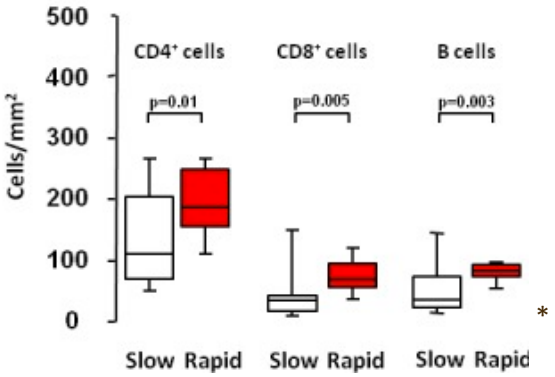
Lung Physiocrine Engineered to Treat Multiple Pulmonary Diseases

ILDs Characterized by T Cell Infiltration

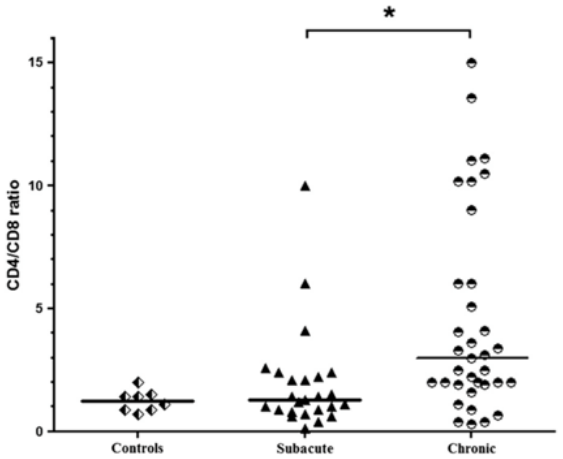
Sarcoidosis



Idiopathic Pulmonary Fibrosis



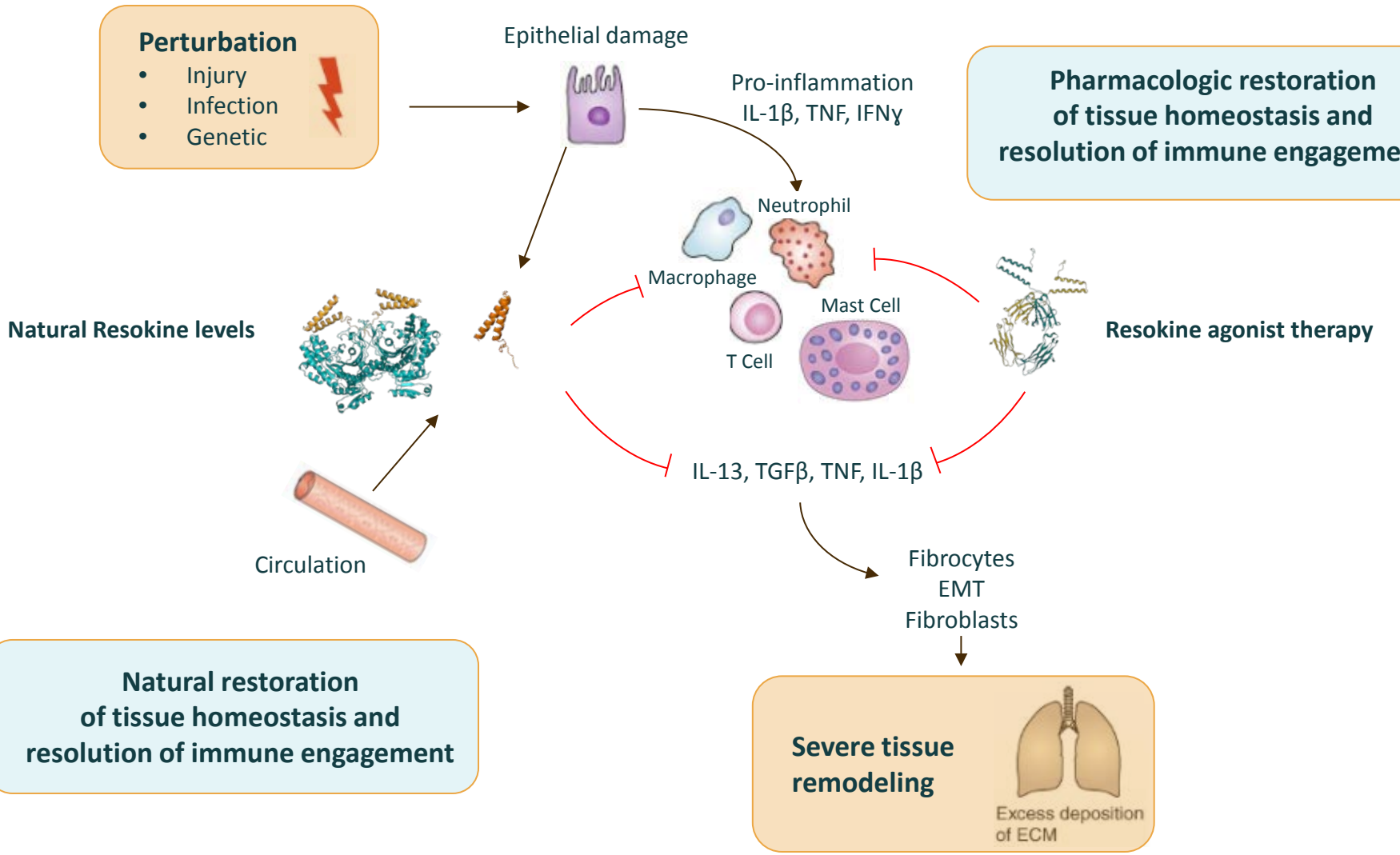
Hypersensitivity Pneumonitis



Balestro et al. PLOS ONE. 2016
Barrera et al.: Functional Diversity of T Cells in HP 2007
Solomon et al. J Bras Pneumol. 2011

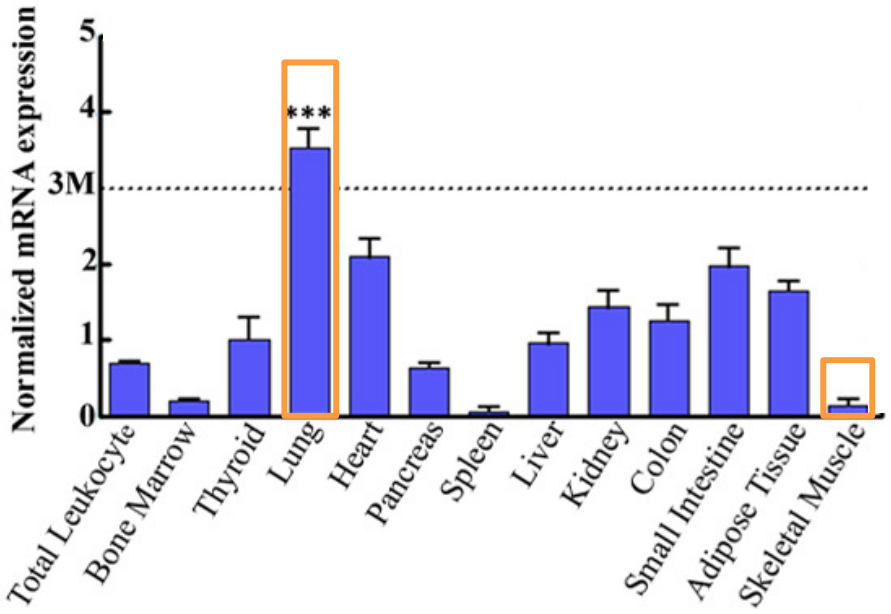
Braun et al. Amer J Resp Crit Care Med 2014

Resokine Promotes Lung Homeostasis



iMod Domain in Lung

Splice Variant Expression Data for iMod in Lung

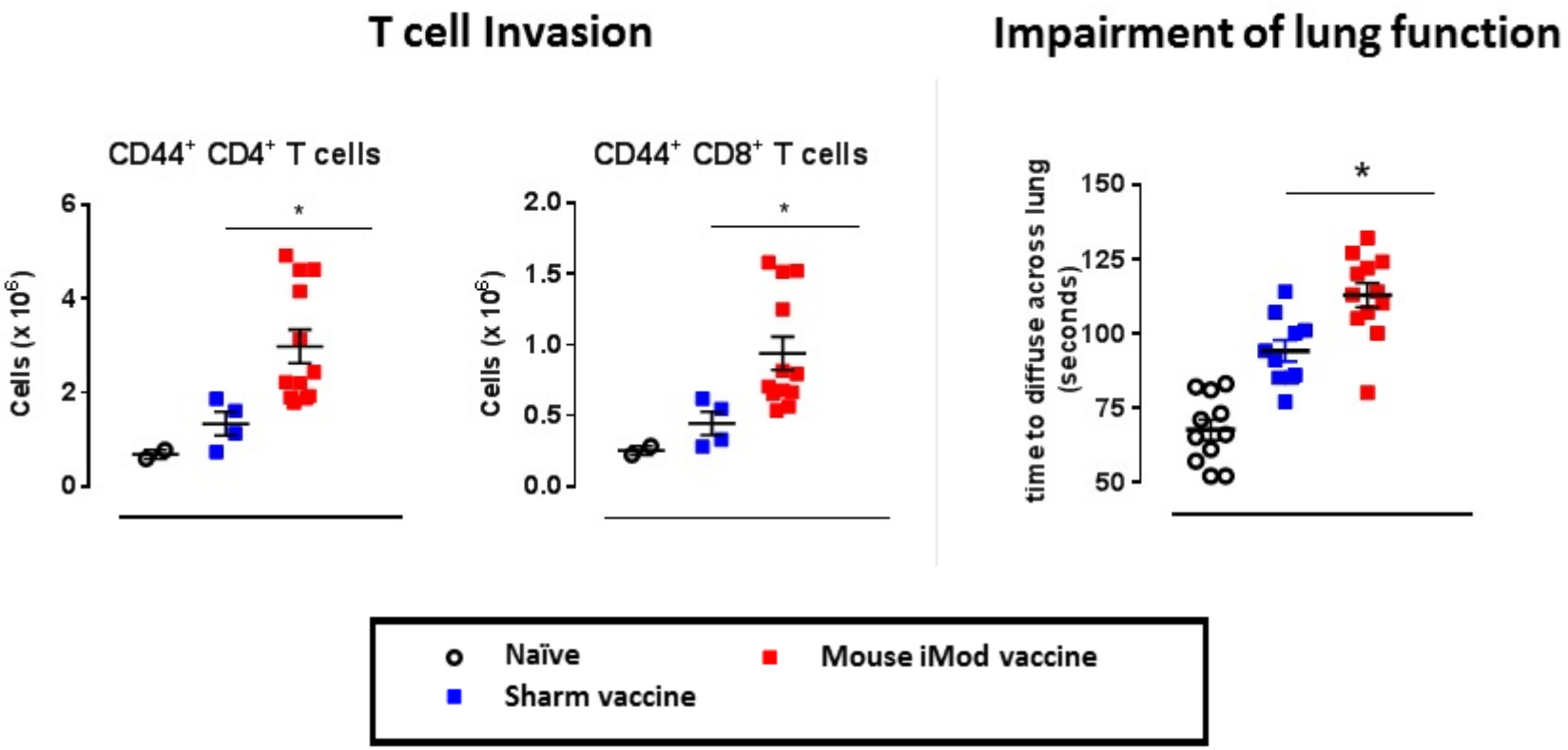


Splice variant for the iMod domain is relatively more expressed in lung than other tissues

Zhou et al. The Journal of Biological Chemistry 2014

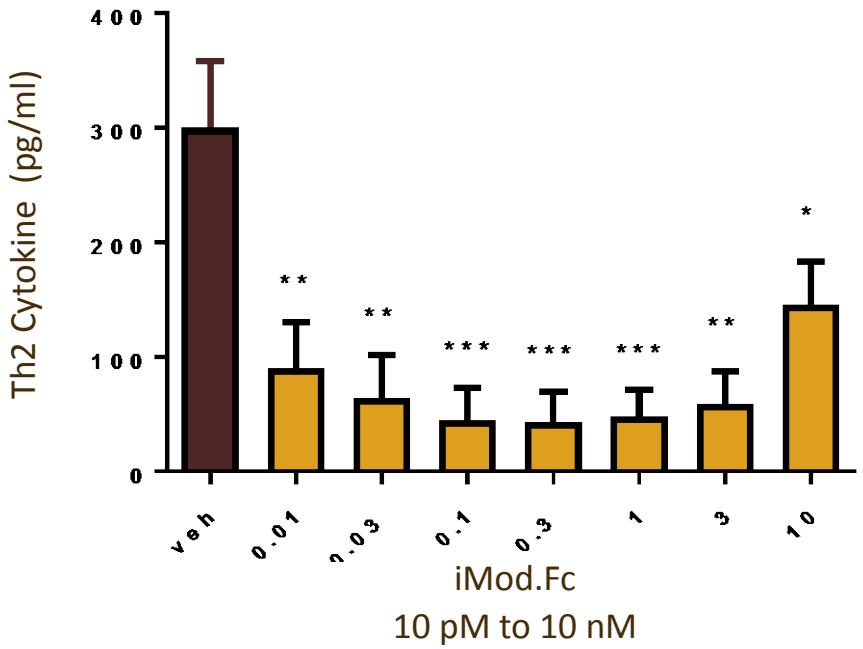
Knockout of Resokine Pathway Increases T Cell Invasion Post Disease Induction

Rodent functional knockout inducing idiopathic pulmonary disease using Bleomycin



* $p < .05$

iMod.Fc Tempers Activated Human T Cells at High Affinity



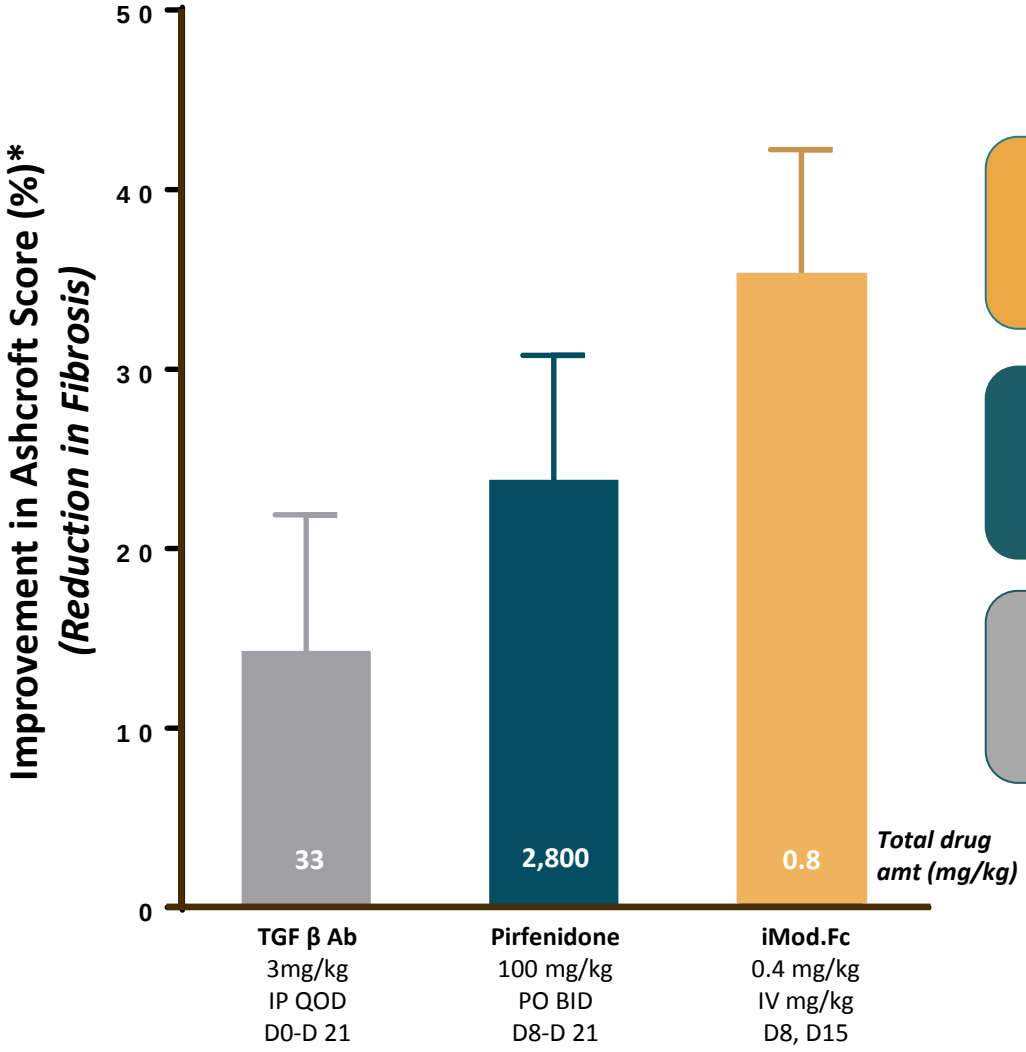
iMod.Fc inhibits Th2 type cytokines from activated T cells

Th2 cytokines play a role in promoting fibrosis in certain interstitial lung diseases

*** p < .001; ** p <.01; * p < .05

iMod.Fc Outperforms Current Treatments

Established Rodent Model for Idiopathic Pulmonary Fibrosis (IPF)



Superior activity
in established IPF fibrotic model

iMod.Fc outperformed pirfenidone
at 1/3500th total dose

Two doses of iMod.Fc
outperformed 11 TGFβ Ab doses

**The Ashcroft scale for the evaluation of bleomycin-induced lung fibrosis is the analysis of stained histological samples by visual assessment*

Significant Untapped Opportunity in ILD

Limited available options for patients

IPF

Irreversable, progressive lung disease

- Chronic progressive fibrotic process
- Acute episodes

Very high unmet medical need

- 2-3 year median survival
- Significant functional and QoL impairment

~135k patients in US

Other ILDs

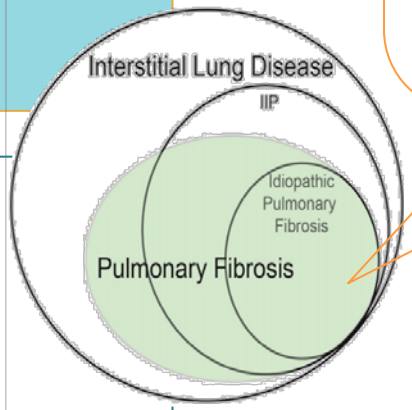
>100 disorders

- Primary & secondary
- Various disease patterns

High unmet medical need

- Heterogeneous, many have grave prognosis
- SOC has limited evidence of safety and efficacy

>450k patients in US across all forms of ILD*



Esbriet

OFEV®

FDA approvals for IPF in 2014

*including IPF

iMod.Fc: Status and 2017 Development Goals

Milestones:

- ✓ Activity in industry proven model of IPF (approved drugs Pirfenidone & Nintedanib)
- ✓ GMP manufacturing kicked off
- ✓ Rat/non-human primate non-GLP safety & PK data support advancement to IND

2017 Development Goals:

- **MOA:** Introduce mechanistic/PD assay
- **IND Enabling:** Complete preclinical safety studies
- **GMP Manufacturing:** Complete initial clinical trial supply
- **Clinical Trial:** Initiate first in human clinical trial


Building a New Class of Therapeutics For Patients
Foundation for the Future

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

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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 2017 Goals and Financial Guidance

2017 Goals

- Partner One or More Programs
- Advance Pipeline with Two Molecules in the Clinic
- Declare 3rd IND Candidate from Physiocrine Discovery Engine

Financial Guidance

- $61.9M cash and investments as of 3/31/2017
- Operations funded into 3Q 2018 without any partnerships
- ~30% expected reduction in operational cash burn compared to 2016*

**Operational cash burn only, excludes cash from financings*