Advancing New Therapeutic Horizons For Patients

Harnessing Novel Physiocrine Biology To Promote Homeostasis

Corporate Presentation
January, 2017

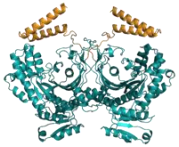
aTyr Pharma
NASDAQ: **LIFE**

Forward-Looking Statements

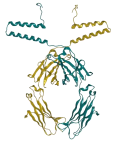
The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “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 Stalaris™, 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 most recent Quarterly Report on Form 10-Q, 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 therapeutic intervention points in homeostasis - **The World of Physiocrines**



Favorable safety profile and potential clinical activity from **1st Physiocrine** program, Resolaris, in 2 rare myopathies



Advancing **2nd Physiocrine** program, Stalaris, into human trials this year

Closing in on a **3rd Physiocrine**-based opportunity as a 2017 IND candidate

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

$76M estimated cash 2016 EOY*
$51M market capitalization 2016 EOY

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

LIFE 2016 Execution

Resolaris (Rare Genetic Myopathies)

- ✓ Adult FSHD: Completed blinded trial, open-label trial, with two ongoing safety extensions
- ✓ Adult LGMD2B: Completed open label trial, with ongoing safety extension
- ✓ Early Onset FSHD: Interim data provided from open label trial, with ongoing safety extension

Goals for Resolaris Development:

- ✓ Not immunosuppressive
- ✓ Favorable safety and tolerability profile in multiple myopathies
- ✓ Active dose at 3.0 mg/kg
- ✓ Narrowed potential efficacy endpoints

Stalaris (Severe Lung Diseases)

- ✓ Additional preclinical model data vs. approved drugs in idiopathic pulmonary fibrosis
- ✓ Non-human primate data
- ✓ GMP manufacturing kicked off

3rd Program (Undisclosed 3rd Attractive Therapeutic Area)

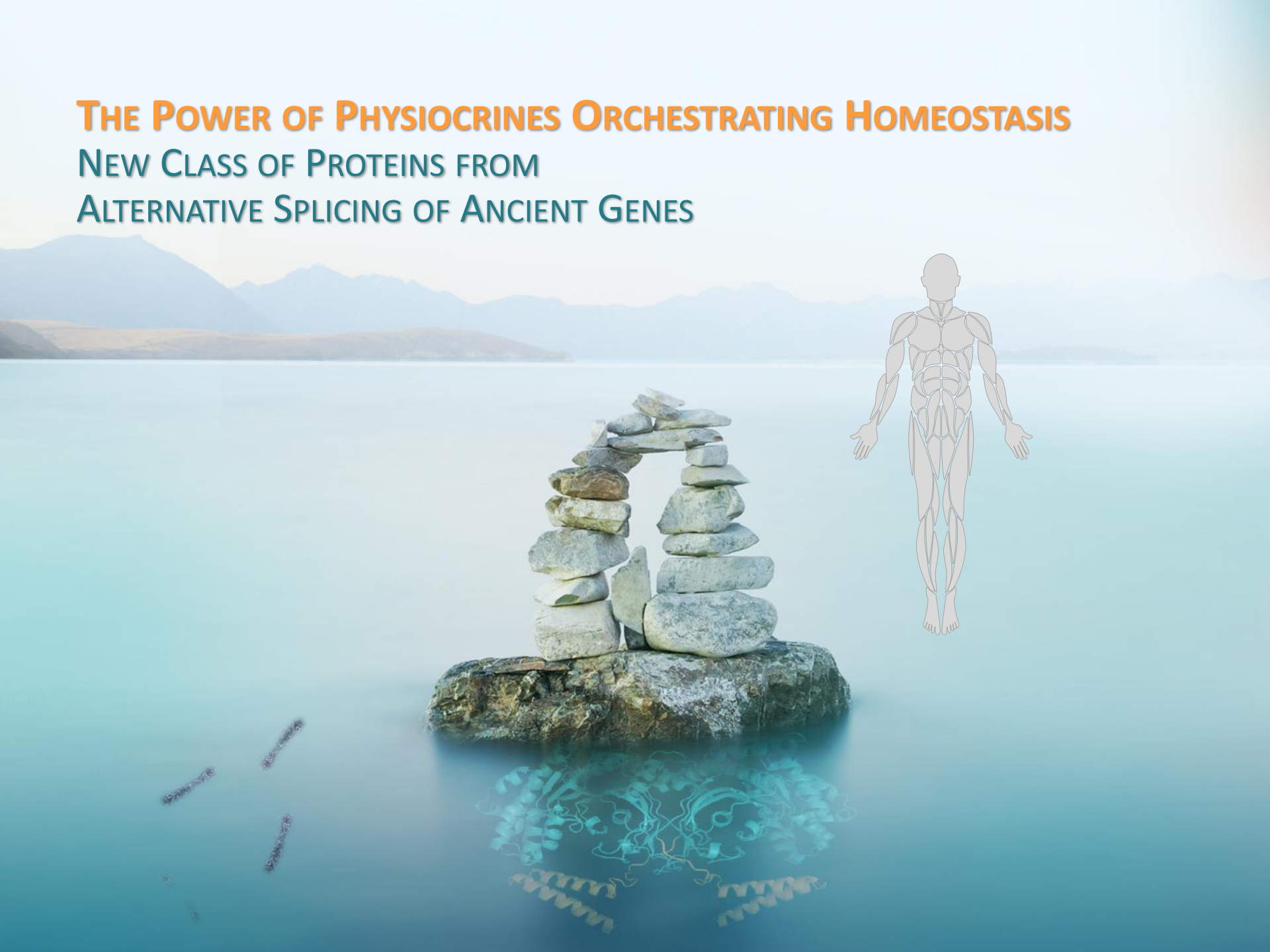
- ✓ 3rd biologics program
- ✓ Lead selection process initiated

Our team executed on milestones on time and under budget

***FSHD** = Facioscapulohumeral Muscular Dystrophy (FSHD). **LGMD2B** = Limb Girdle Muscular Dystrophy 2B.*

The Power of Physiocrines Orchestrating Homeostasis

New Class of Proteins from Alternative Splicing of Ancient Genes



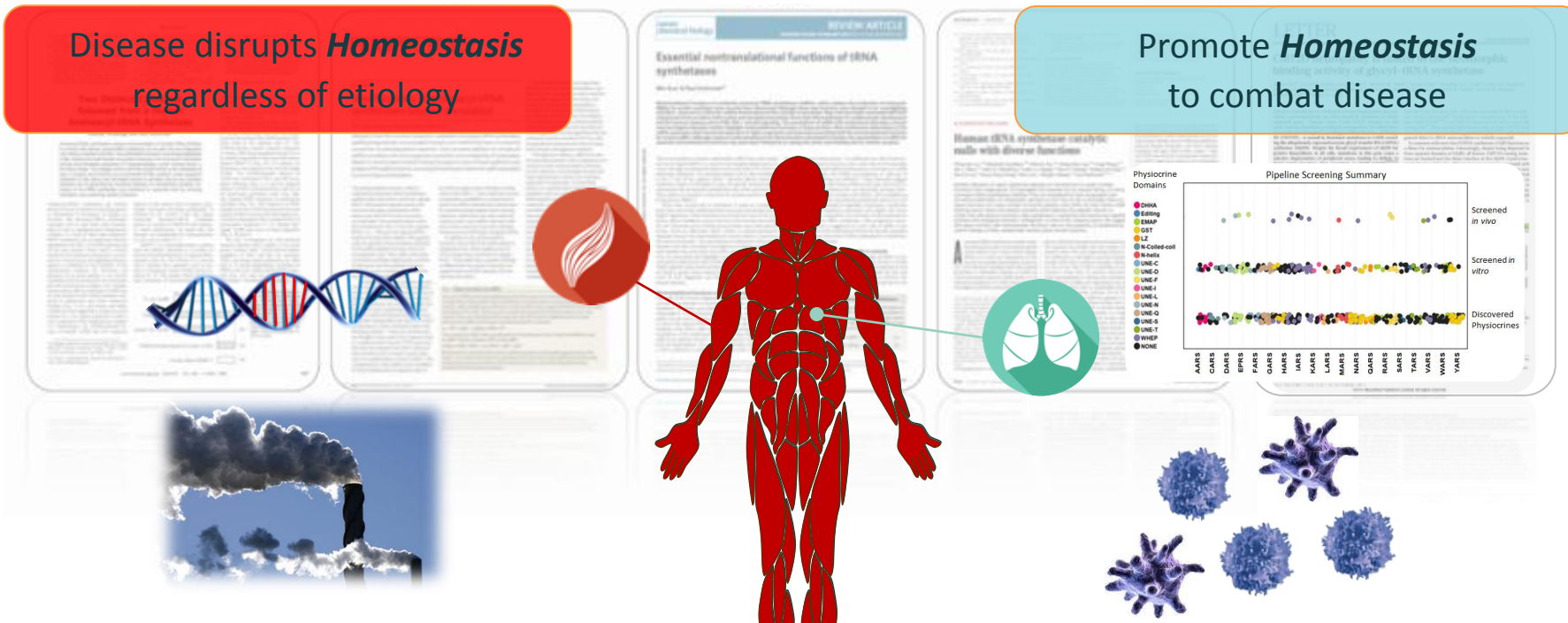
Orchestrating Homeostatic Pathways for Novel Therapies

Discovery of potential therapeutic intervention points

Science 1999 | Nature 2010 | Nature 2013 | Science 2014 | Nature 2015

Disease disrupts ***Homeostasis*** regardless of etiology

Promote ***Homeostasis*** to combat disease

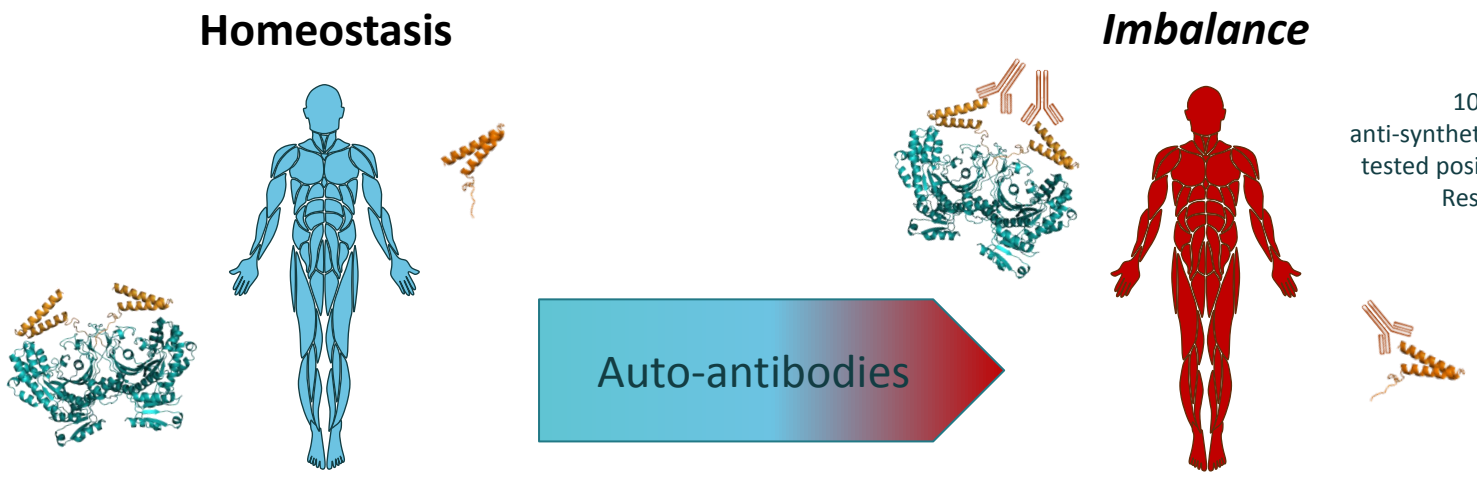


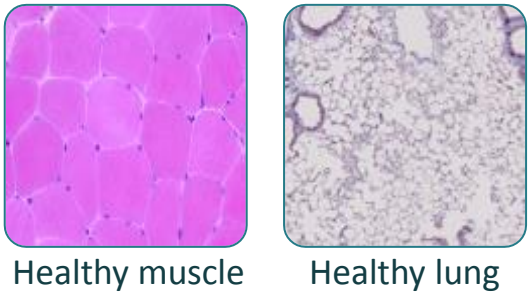
2015 value of therapeutic intervention points:
>$25B global sales for TNF antagonists
>$27B global insulin agonist market

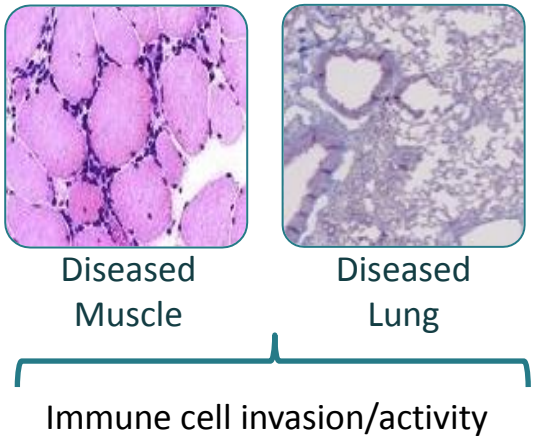
Physiocrines may promote homeostasis and provide for novel therapeutic intervention points for better efficacy and safety

Evidence for Homeostatic Role of a Physiocrine in Humans

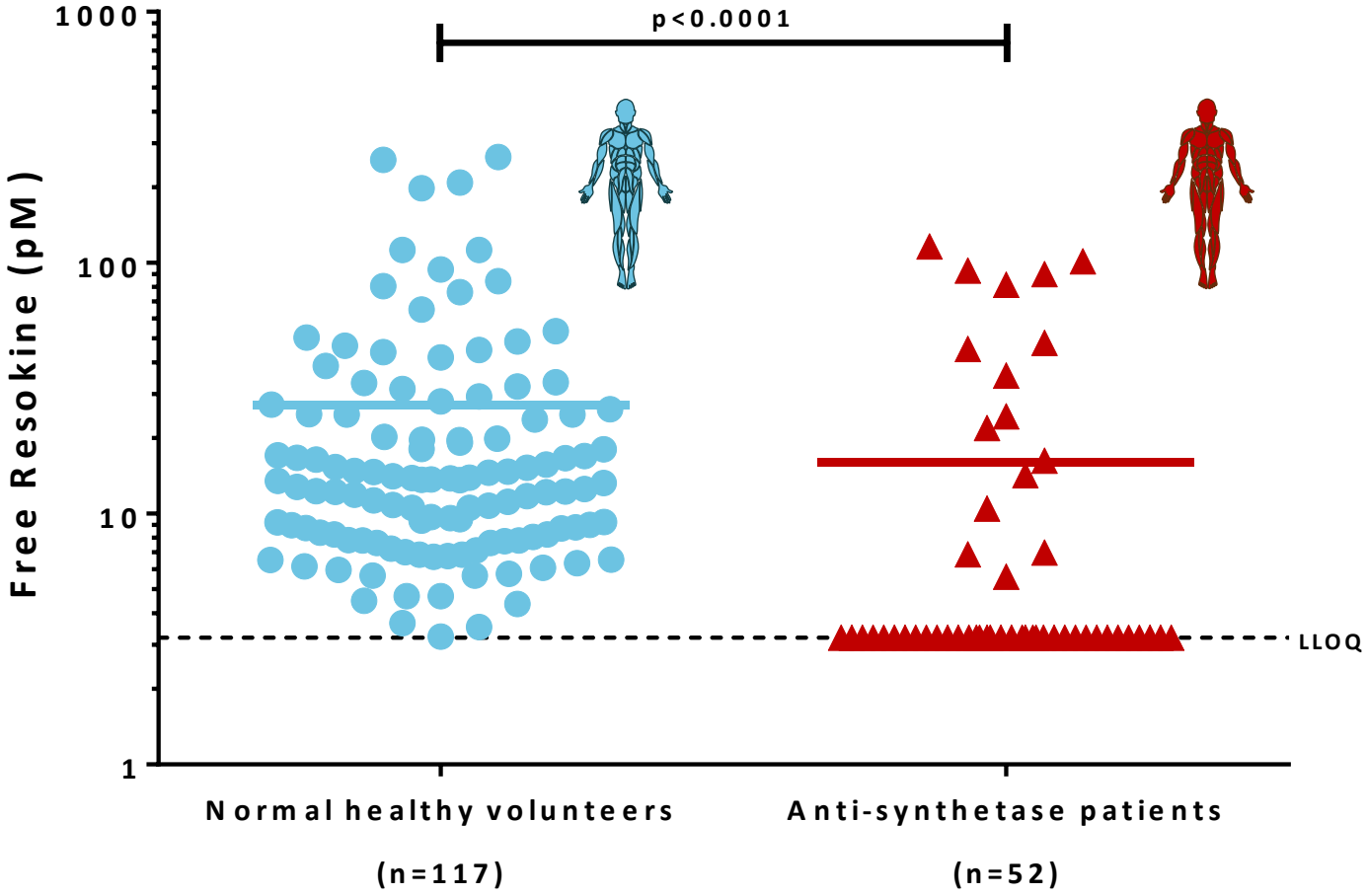
Disrupting the Resokine Pathway Promotes Muscle and Lung Disease







Free Resokine Pathway in Anti-Synthetase Patients Diminished



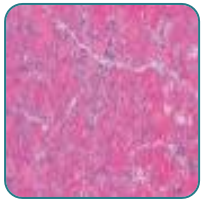
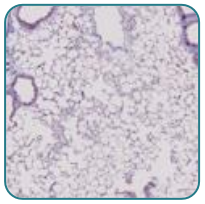
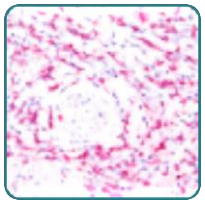
69% at or below limit of detection

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.

Resokine: 1st Physiocrine Pathway Harnessed

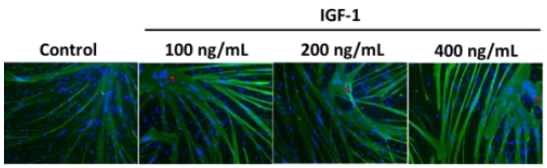
"Resolution of immune activity"

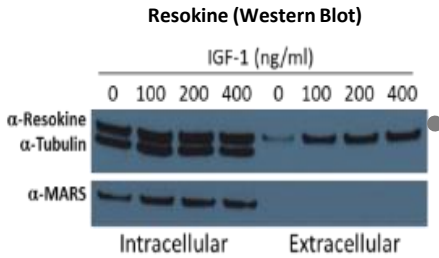
Muscle
Resokine pathway relates to a secreted 57kD protein from skeletal muscle (full length HARS*)

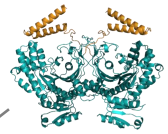
Lung
Resokine pathway relates to a 7kD protein (the iMod domain, a splice variant of HARS)

MOA
- Involved in muscle differentiation
- Tempers activated T cell response

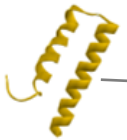
MOA
- Lung expression >> skeletal muscle
- Tempers activated T cell response



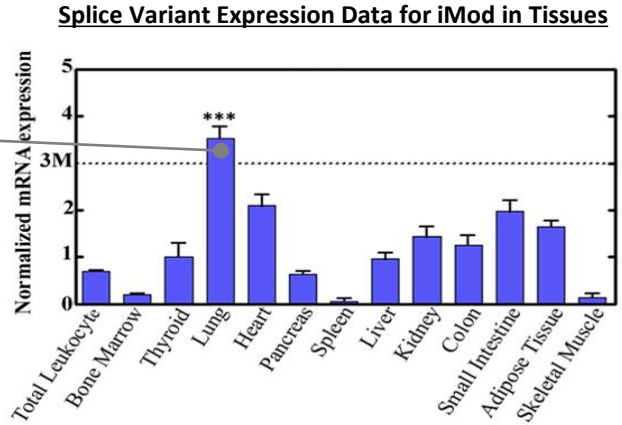




Resokine



iMod Domain



**HARS or histidine aminoacyl tRNA synthetase is a single gene responsible for a series of Physiocrine proteins*

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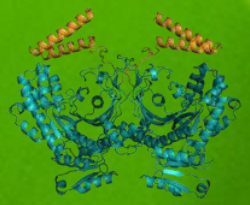


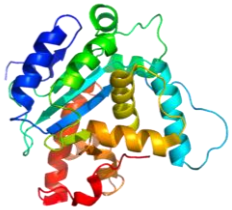
RESOLARIS

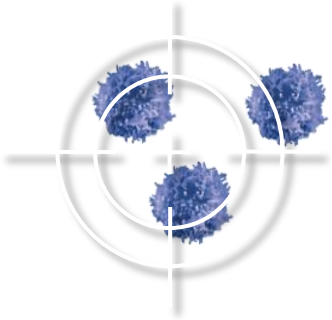
HARNESSING THE RESOKINE PATHWAY TO TREAT MULTIPLE RARE MUSCLE DISEASES

Rare Myopathies with an Immune Component (RMIC)

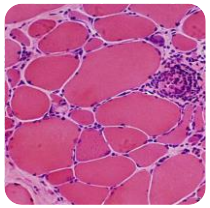
Chronic damage, homeostasis disrupted

Untapped therapeutic intervention point

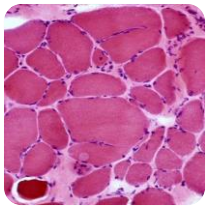




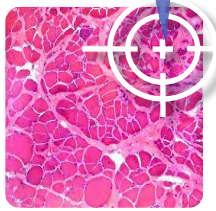
Genetic Mutation	Aberrant Protein Expression	Localized T Cell Invasion/Proliferation
FSHD	Multiple proteins	
LGMD2B	Dysferlin proteins	
DMD	Dystrophin proteins	



FSHD



LGMD2B



DMD

Potential to link genotype to specific T cell phenotype

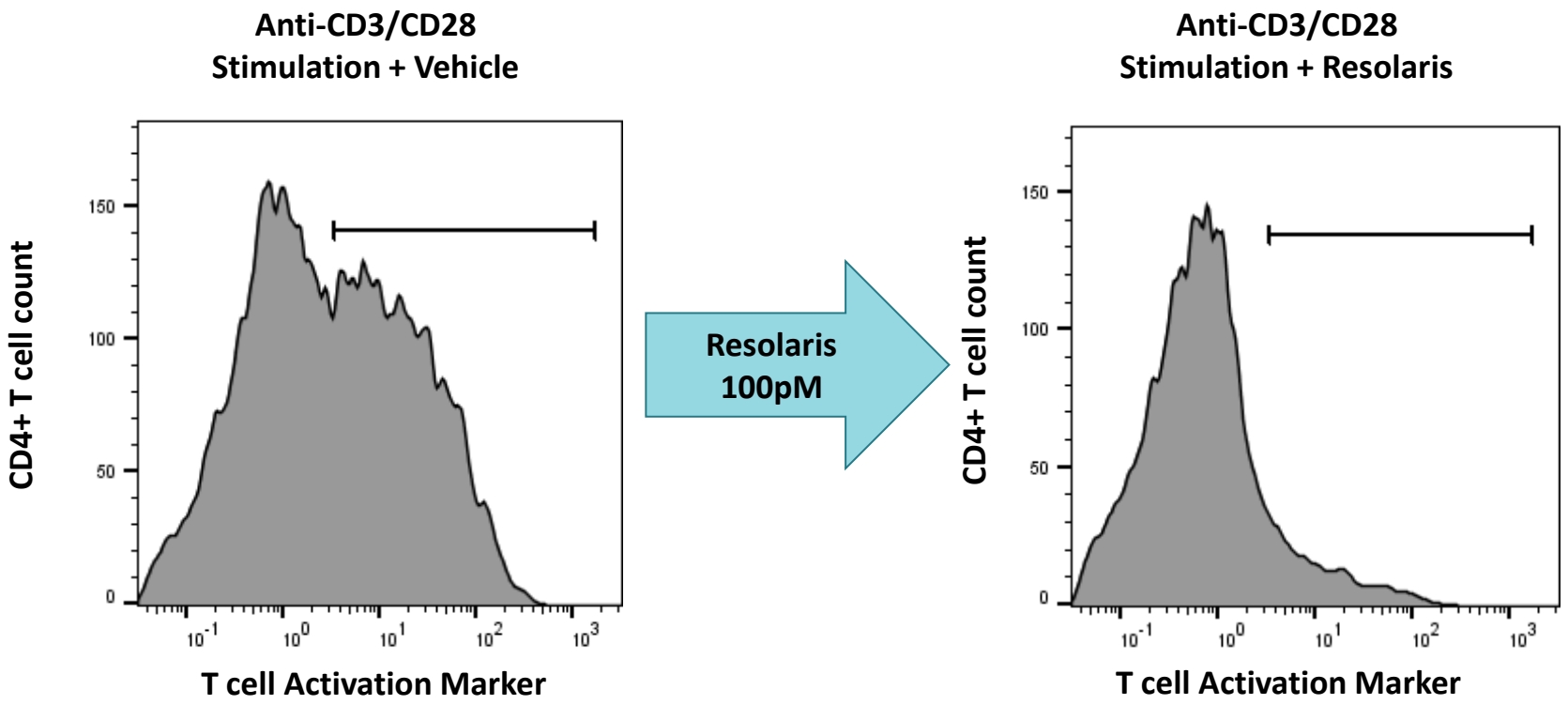
Frisullo et al., J. Clin. Immunol., 2011. Gallardo et al. Neurology, 2001. Flanigan et al. Human Gene Therapy, 2013.

***FSHD** = Facioscapulohumeral Muscular Dystrophy (FSHD). **LGMD2B** = Limb Girdle Muscular Dystrophy 2B.*

***DMD** = Duchenne Muscular Dystrophy.*

Resolaris Tempers Activated T cells

Demonstrated effect as an immuno-modulator

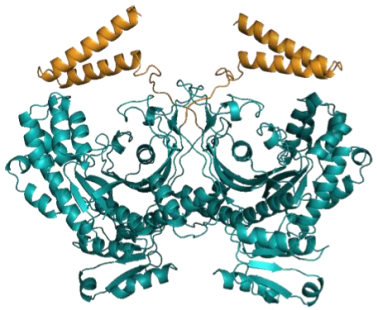


*Resolaris appears to work on **activated** T cells*

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*

First Physiocrine For Patients: Resolaris



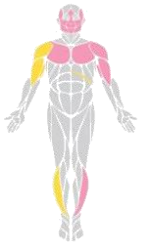
Derived from a naturally occurring protein, the histidine aminoacyl tRNA synthetase **(HARS)**

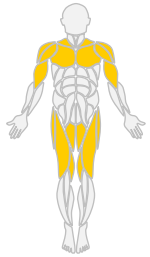
- Skeletal muscle secretes Resokine
- Resokine, an agonist, plays a role in homeostasis & T cell responses in muscle
- Recombinant version of Resokine
- Demonstrated favorable safety profile and potential clinical activity in two rare myopathy indications
- Therapeutic potential for rare myopathies with an immune component (RMIC), **over 20** potential indications

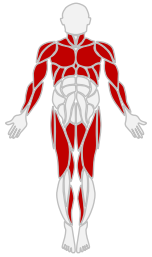
➢ **Strategy:** Establish broad utility across multiple indications

Few Treatment Options: FSHD, LGMD2B, & DMD

	FSHD	LGMD2B	DMD
Genetics	Toxic gain of function (DUX4 region)	Loss of function mutations (Dysferlin gene)	Loss of function mutations (Dystrophin gene)
Immune Pathology	Immune infiltration[1] by activated T cells ($CD8^+$)	Immune infiltrates[2] of $CD4^+$, $CD8^+$ and macrophages	Immune infiltrates[3] of $CD4^+$, $CD8^+$
Clinical	Debilitating, progressive skeletal muscle weakness Pain, fatigue, difficulty moving limbs, may have respiratory distress		Similar clinical symptoms to FSHD and LGMD2B, with potential severe cardiac weakness and effects, and higher morbidity
Standard of Care	No therapeutic treatments, only supportive care provided		Steroids and recently approved exon specific drugs
Disease Progression	Heterogeneous by muscle	Homogeneous by muscle group	Homogeneous, steeper slope, by muscle groups







[1]*Frisullo et al. J Clin Immunol (2011) 31:155–166*
[2]*Gallardo et al. Neurology 2001;57:2136–2138; Yin et al. Int J Clin Exp Pathol 2015;8(3):3069-3075*
[3]*Flanigan et al. Human Gene Therapy, 2013. Yin et al. Int J Clin Exp Pathol 2015.*

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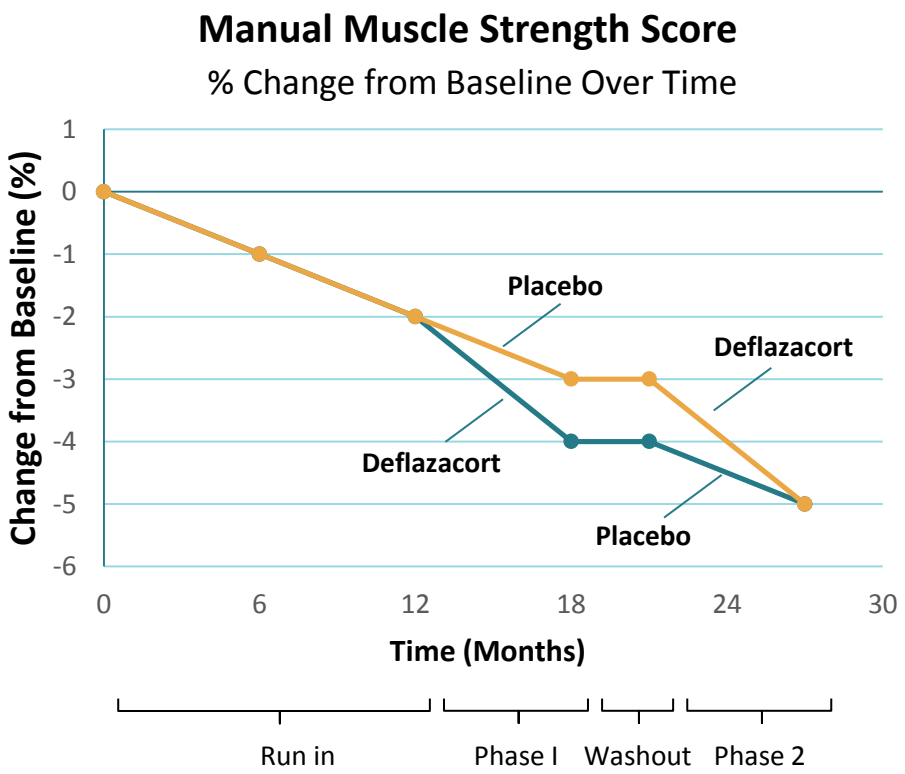
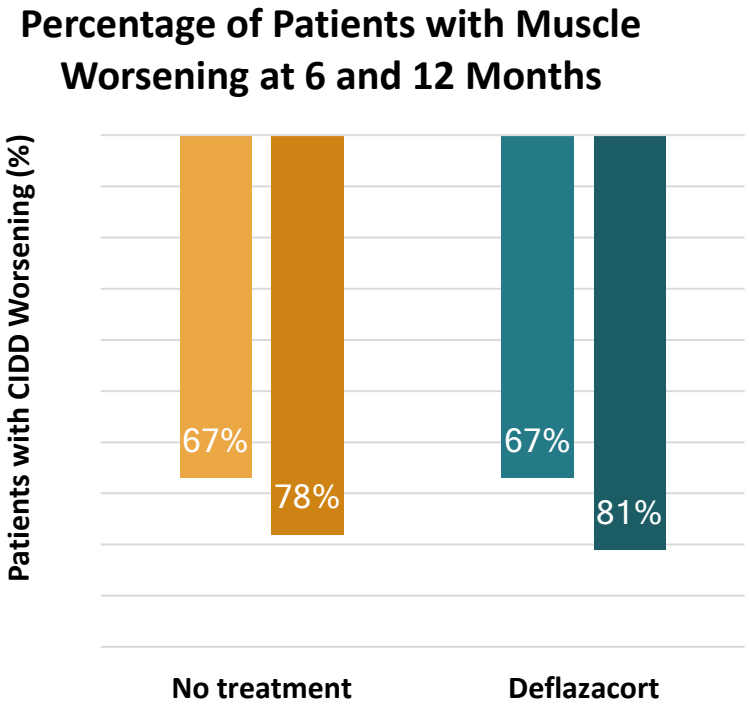
LGMD Patients Manual Muscle Strength Progressively Declines





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

Resolaris Phase 1b/2 Clinical Trials

Objectives

Evaluate Safety and Tolerability

- ✓ Build safety dossier for Resolaris
- ✓ Multiple indications, different dosing regimens, longer duration

Evaluate Potential Activity Assessments*

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

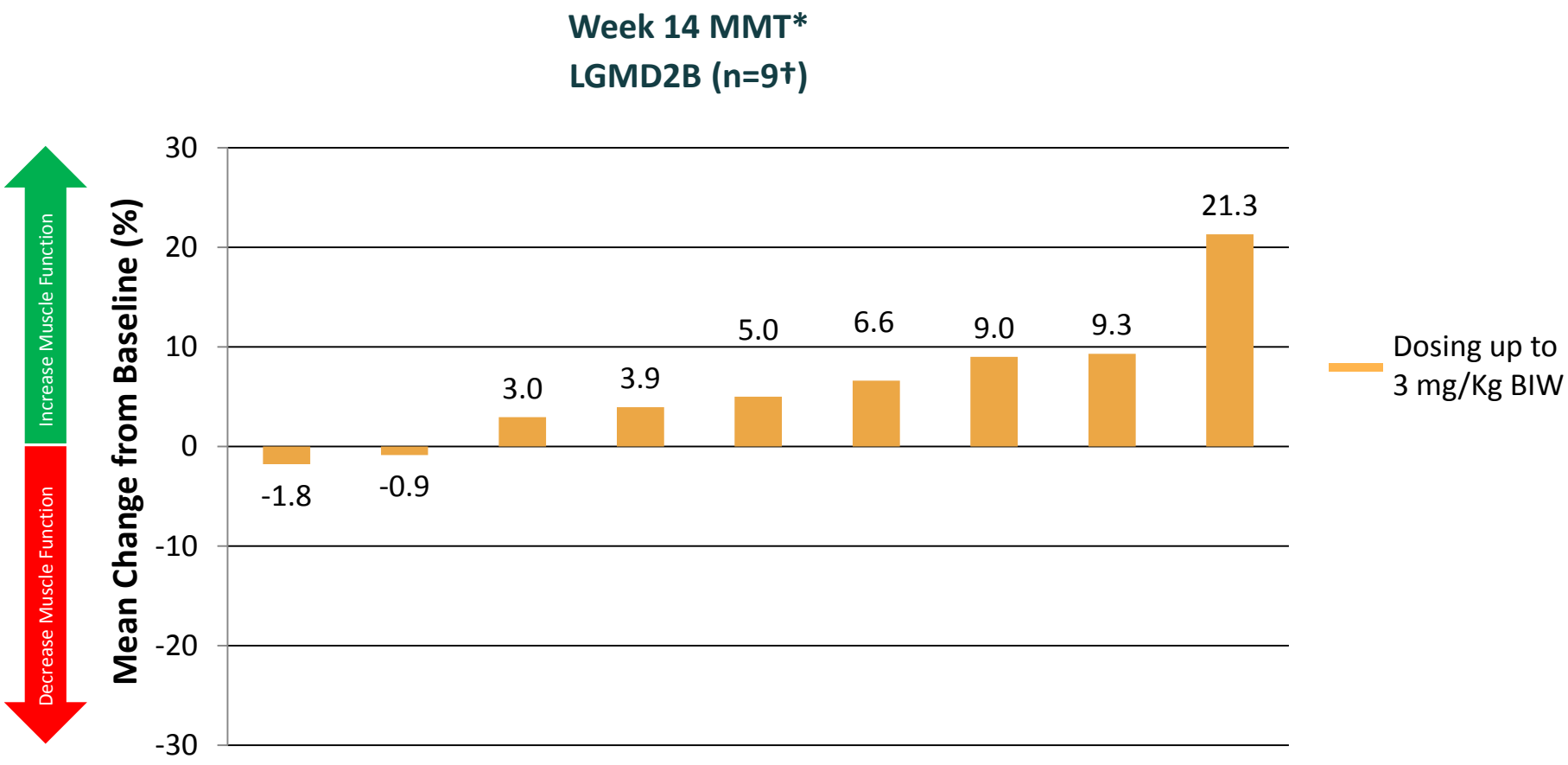
Trial	Indication(s)	Patients	Highest Dose	Design
002	Adult FSHD	3 dose cohorts (n=20 Total)	3.0 mg/kg Weekly (12 weeks)	Placebo controlled, Double blinded; Interpatient Dose Escalation up to 12 weeks
003	Early onset FSHD	Stage 1 (n=8)	3.0 mg/kg Weekly (6 weeks)	Open-label, Intrapatient Dose Escalation for 12 weeks
004	Adult LGMD2B, Adult FSHD	LGMD2B (n=10) FSHD (n=8)	3.0 mg/kg Biweekly (4 weeks)	Open-label, Intrapatient Dose Escalation for 12 weeks

**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

MMT Scores LGMD2B Patients (004 Trial)

Individual Patient Changes from Baseline (%)



1-week follow-up is earlier than week 14 for 2 early discontinuations

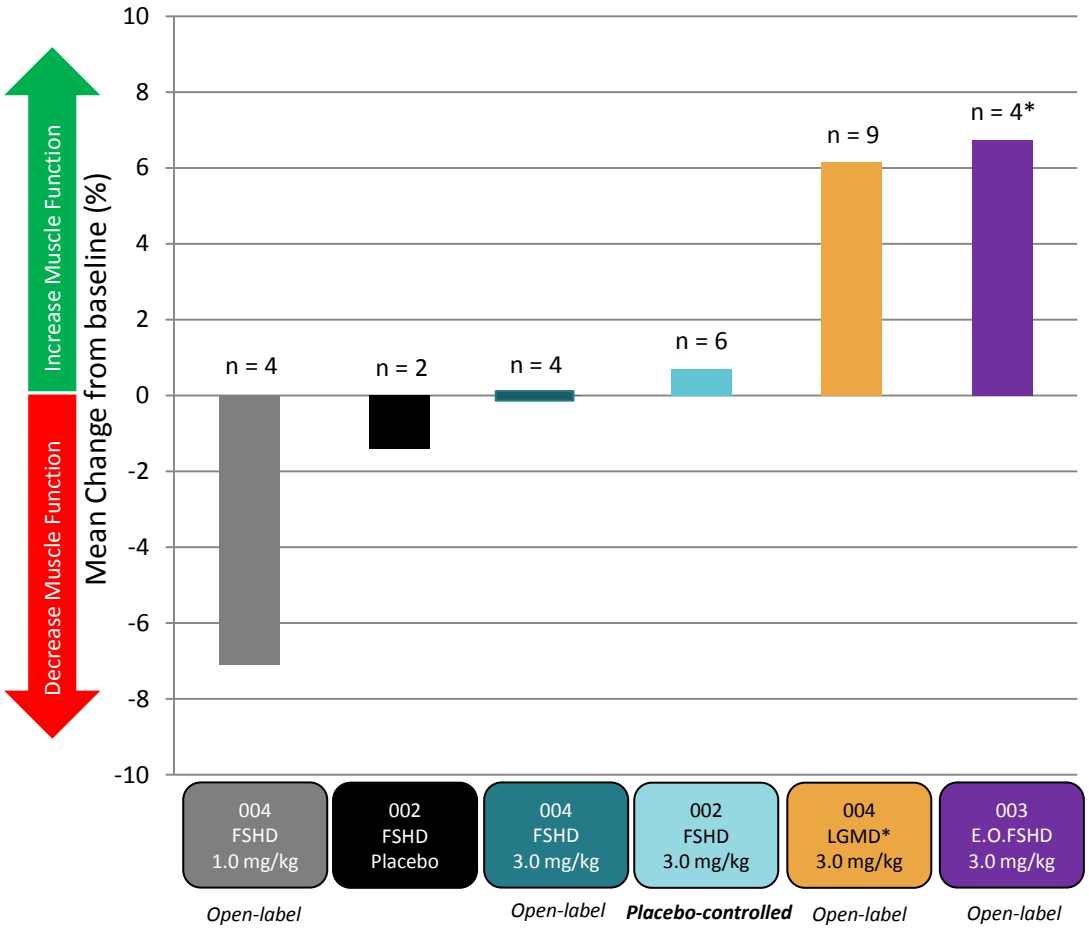
† One patient in 004 Trial did not have an MMT measurement due to being wheelchair bound at baseline

Relatively Stable or Improved Muscle Function Observed

Change from baseline overall MMT scores at week 14

Overall Mean MMT Change Week 14 by Dose Group

FSHD & LGMD2B Patients From 002, 003, 004 Trials



Manual Muscle Testing (MMT):
A measure of muscle function/strength

50% to 78% of patients in Resolaris dose groups had increased MMT scores

No placebo patients had increased MMT scores

3.0 mg/kg weekly identified as an active dose

**Early onset FSHD (003) Trial represents interim data results (4 patients of a total of 8)*

Robust Safety & Tolerability Dossier

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

No observed immuno-suppressive effects: consistent with a homeostatic pathway

Resolaris demonstrated a favorable safety profile and was generally well-tolerated across all doses tested in multiple myopathies, various age-groups, and with long-term exposure

No Serious or Severe adverse events were reported by study investigators

No clinical symptoms observed with low-level anti-drug antibody assay signals and protocol discontinuations were primarily driven by transient infusion related reactions

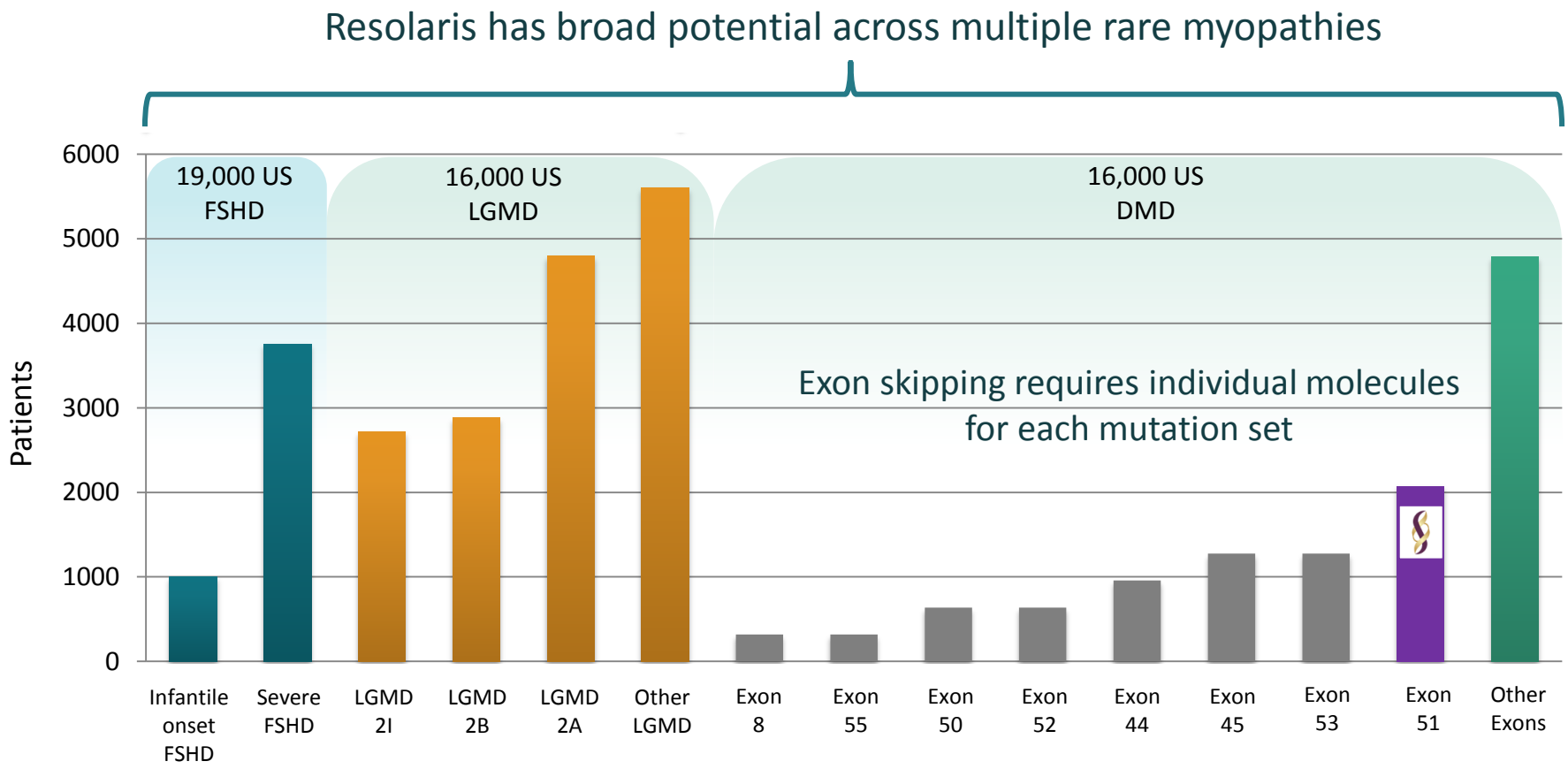
Going Forward: Target Product Profile (Discontinuation Rate ≤ 10%)

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

FDA lifted partial clinical hold for dosing above 3.0 mg/kg

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

Clinical Status

- ✓ Established a favorable safety profile and identified an active dose
- ✓ Signals of clinical activity across (1) LGMD2B (2) FSHD and (3) Early onset FSHD
- ✓ Commercial scale manufacturing poised for future trials

2017 Development Goals

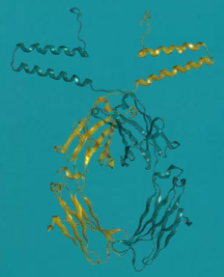
First Half

- **Clinical Results:** Early Onset FSHD Patients (003)
- **Regulatory:** Advance interactions with regulatory agencies
- **Biomarker/MOA:** Introduce Mechanistic/PD Assay

Second Half

- **Clinical Trial:** Kick off next trial post partnership*

**Partner for one or more programs*



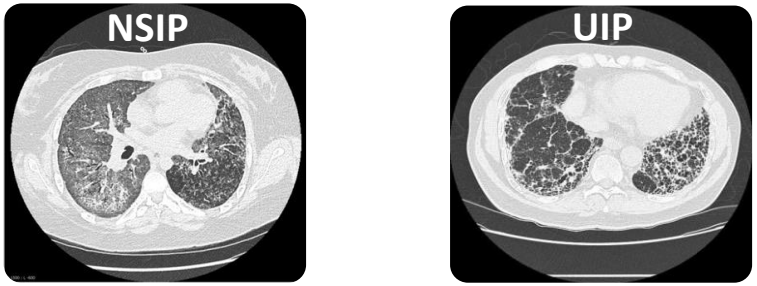
STALARIS

LUNG PHYSIOCRINE ENGINEERED TO TREAT MULTIPLE PULMONARY DISEASES

Interstitial Lung Disease Opportunity

Driven by a combination of immunological and fibrotic pathways

PATIENTS
UNMET NEED

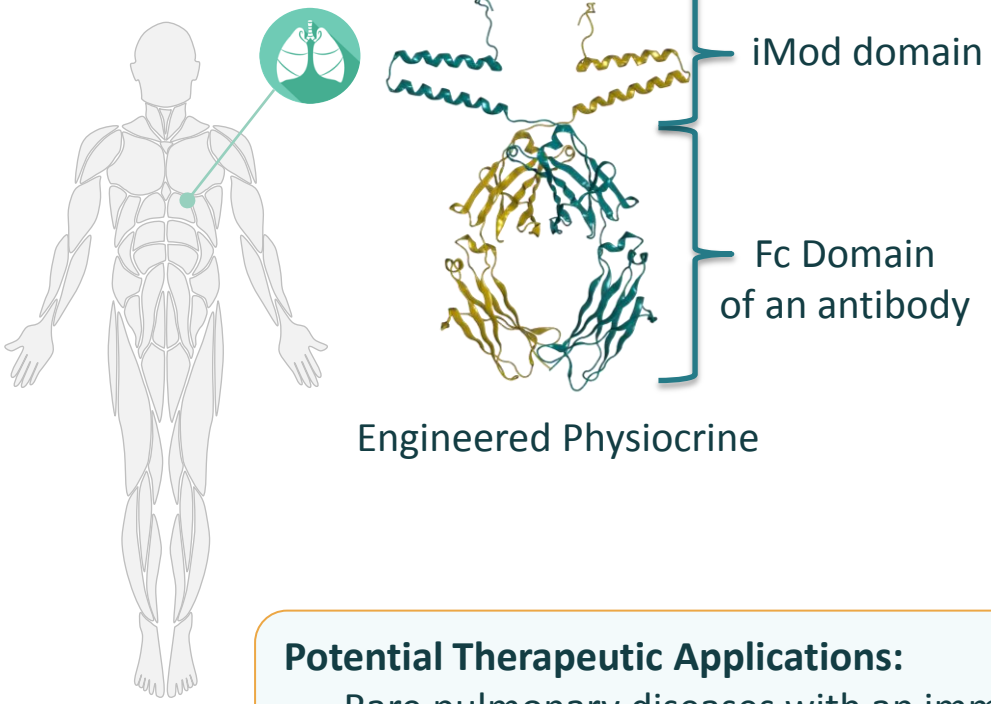
Interstitial Lung Disease (ILD)	Over 100 different specific disease types
Standard of Care	Steroids and immuno-suppressants Approved therapies for IPF*: Pirfenidone & Nintedanib
Pathology	
Pattern of Disease	 Pattern of disease, e.g. usual interstitial pneumonia (UIP) vs. non-specific interstitial pneumonia (NSIP), to determine diagnosis/prognosis
Prognosis	Poor prognosis for these patients e.g. 2-3 year median survival for IPF

Adapted from: Thannickal VJ, et al. Ann Rev Med. 2004;55:395-417 (and) 2013 ATS Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias

***IPF =** Idiopathic Pulmonary Fibrosis*

Stalaris Program: Opportunity for Lung Patients

Leverages Knowledge of Resokine Pathway in Lung



Engineered Physiocrine

- **iMod domain:** Resokine splice variant relatively more expressed in ***lung*** than other tissues
- **Fc Domain:** increased exposure to potentially enable ***once-monthly dosing in humans***
- **Engineered result:** Stalaris ~350x increased exposure vs. iMod; while retaining T cell modulation activity
- **1st molecule** from internal Fc platform

Potential Therapeutic Applications:

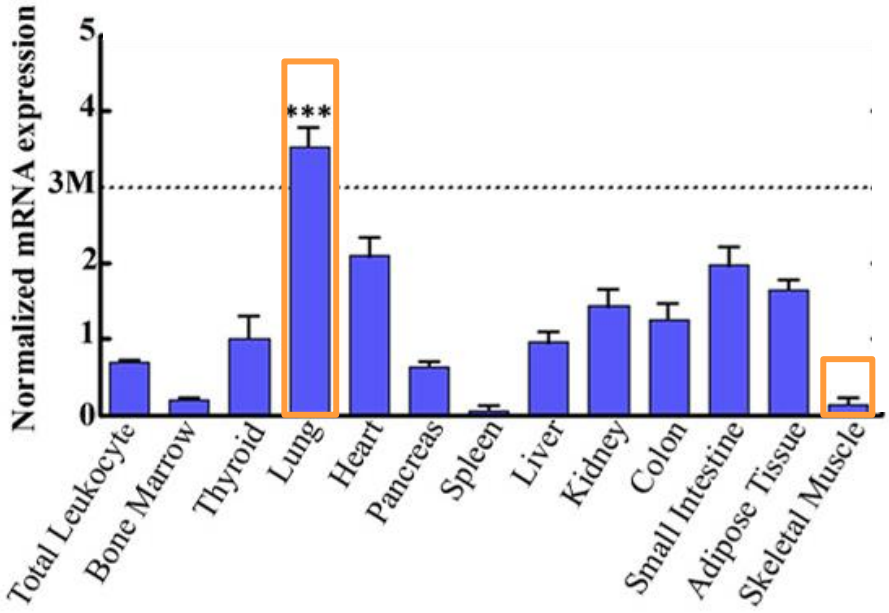
Rare pulmonary diseases with an immune component (RPICs)

Broader reach into RPICs and interstitial lung disease (ILD) indications

Stalaris from Greek, statera for balance

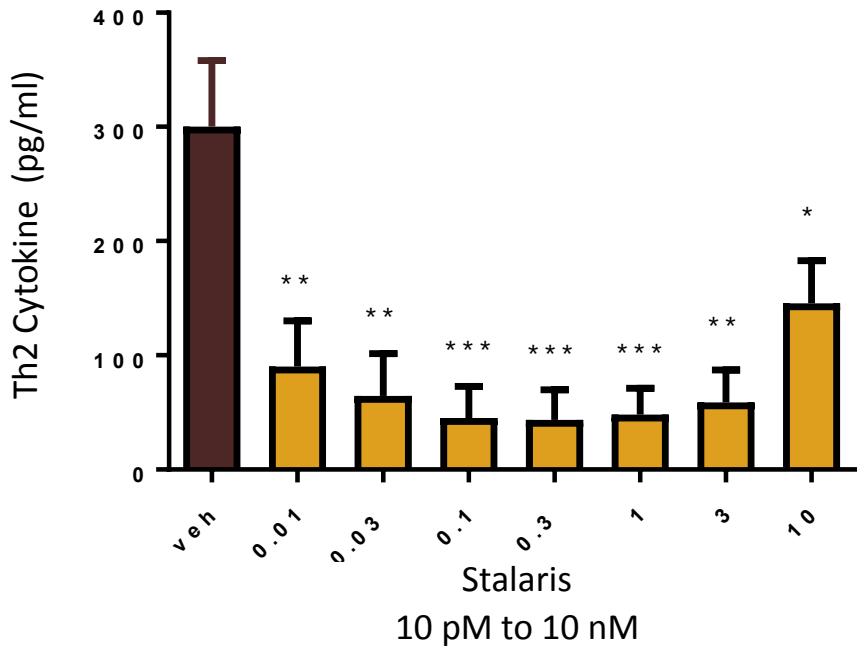
iMod Domain in Lung

Splice Variant Express Data for iMod in Lung



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

Stalaris Tempers Activated T Cells at High Affinity

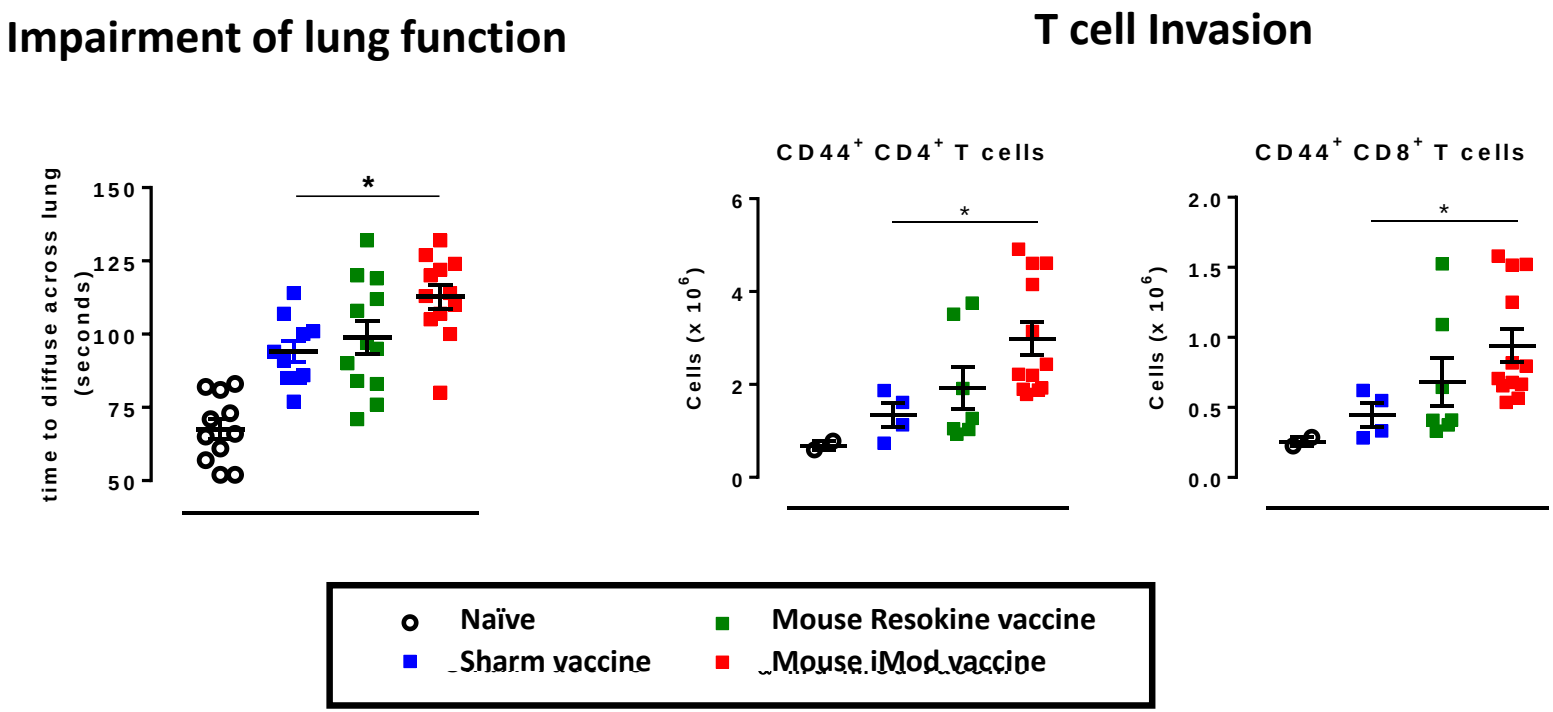


- Stalaris inhibits Th2 type cytokines from activated T cells
- Th2 cytokines play a role in promoting **fibrosis** in certain interstitial lung diseases

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

Knockout of Resokine Pathway Increases T Cell Invasion Post Disease Induction

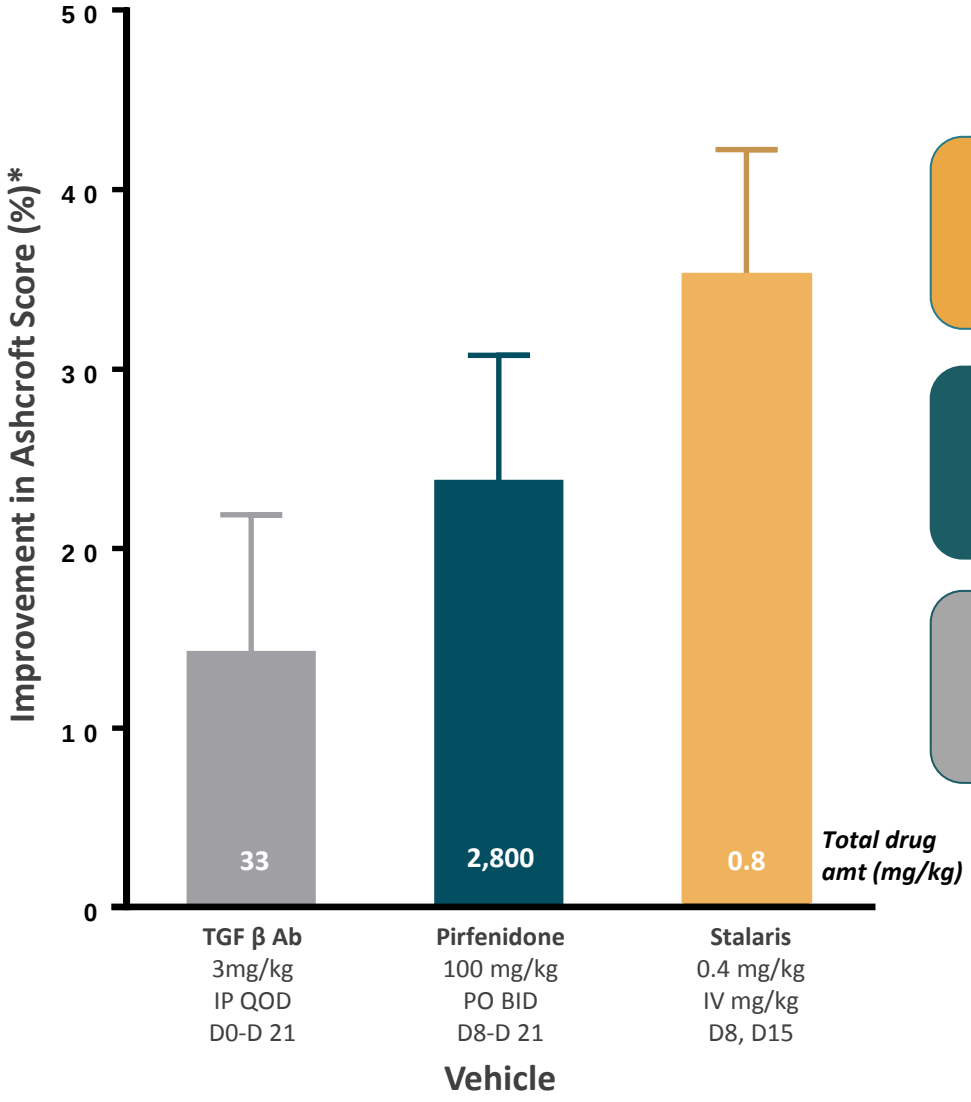
Rodent functional knockout inducing idiopathic pulmonary disease using Bleomycin



** p < .05*

Stalaris Outperforms Current Treatments

Established Rodent Model for Idiopathic Pulmonary Fibrosis (IPF)



Superior activity
in established IPF fibrotic model

Stalaris **outperformed pirfenidone** at **1/3500th** total dose

Two doses of Stalaris **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*

Stalaris: Status and 2017 Development Goals

Preclinical Status:

- ✓ 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:

First Half

- **Biomarker/MOA:** Introduce mechanistic/PD assay
- **IND Enabling:** Initiate preclinical safety studies

Second Half

- **GMP Manufacturing:** Complete 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

Grove Matsuoka
SVP, Product Programs and Planning

Ashraf Amanullah, Ph.D.
VP, Manufacturing

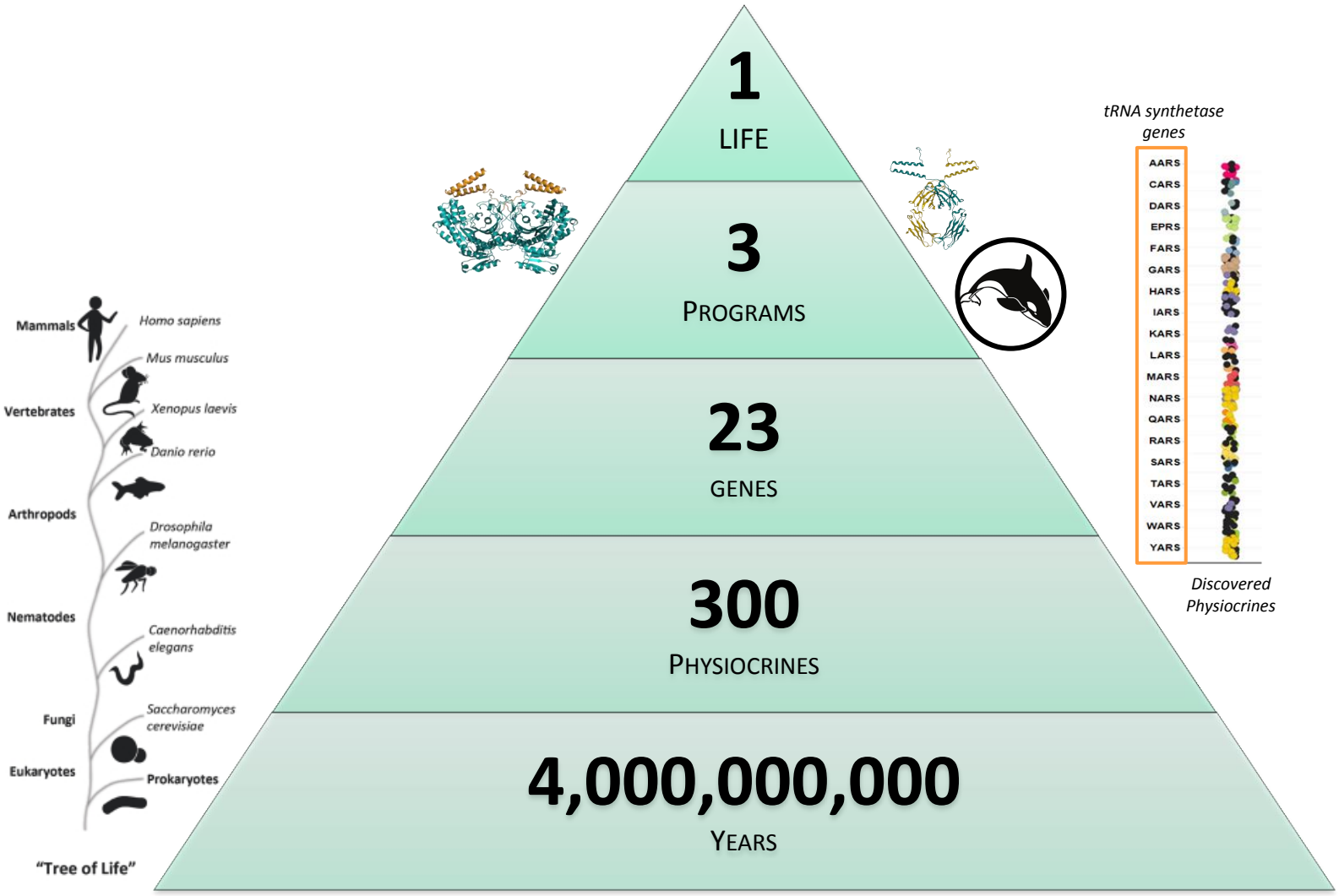
Andrea Cubitt, Ph.D.
VP, Product Protection

John Blake, CPA
VP, Finance

Holly D. Chrzanowski
VP, Enterprise Talent and Organization

Nancy Krueger
VP, Legal Affairs

LIFE Numbers



aTyr Pharma

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

- $76M estimated cash 2016 EOY*
- Operations funded into 3Q 2018 without any partnerships
- ~30% expected reduction in operational cash burn compared to 2016**

**Estimated cash, cash equivalents, and investments provided pending completion of year-end financial close and external audit*
***Operational cash burn only, excludes cash from financings*


THANK YOU!