A novel mechanism for treating Idiopathic Pulmonary Fibrosis (IPF) using small molecules

Mehran F. Moghaddam, PhD, MBA

CEO

memo@oroxbios.com

World Orphan Drug Congress

April 26, 2018

Washington, DC

OROX BioSciences, Inc.
Novel Drugs for Unmet Medical Needs

www.oroxbios.com

The Company

OROX BioSciences, Inc.
Novel Drugs for Unmet Medical Needs

A San Diego biotechnology start-up dedicated to discovery and development of novel drugs to treat fibrotic diseases

The Team

GREGORY REYES
MD, PhD – COO/CMO
Former Sr. VP of Global Drug Discovery
Celgene (also, Schering-Plough, Pfizer, Biogen)

BRUCE D. HAMMOCK
PhD – Chairman of Scientific Advisory Board
Distinguished Professor in UC-Davis Comprehensive Cancer Center. Member of the National Academy of Sciences and the National Academy of Inventors.

MEHRAN F. MOGHADDAM
PhD, MBA – CEO
Former Head of Discovery DMPK
Celgene (also, Pfizer, DuPont)

The Team

NICHOLAS KENYON

MD, MAS – Pulmonary Disease.

Professor of Medicine and Chief of Division of Pulmonary, Critical Care, and Sleep Medicine at UC-Davis School of Medicine.

NEIL RAHEJA

PhD – Medicinal Chemistry.

Former Associate Director in Dept of Medicinal Chemistry at Celgene. As a consultant, he enabled 3 programs for multiple companies and moved them into lead optimization and early development. (also, Pfizer)

EKIHIRO SEKI

MD, PhD – Fibrosis.

Dr. Seki is currently conducting his basic and translational research focusing on matrix-mediated liver fibrosis, alcoholic and nonalcoholic fatty liver disease, and liver malignancy at Cedars-Sinai Medical Center.

JOHN IMIG

PhD – Eicosanoid Biology.

Professor and Director of the Drug Discovery Center in the Department of Pharmacology & Toxicology at the Medical College of Wisconsin studying fatty acids “eicosanoids” influence on kidney and cardiovascular function.

The Team

WILLIAM KACHIOFF
Financial Affairs.
Former SVP and CFO of Biocept. (also, Althea, Deloitte & Touche, Abbott Laboratories, Clarient, Vivus and Cutera)

KENNETH J. ROLLINS
JD, Corporate Counsel
A partner at Cooley LLP representing emerging and late stage private companies and public companies in a wide range of corporate and securities matters. Ken is counsel to companies in diverse industries, including biotechnology ranging from startups to public companies.

Specific Aims

Attack pathophysiological mechanisms underlying fibrosis

(stand-alone or in combination with existing therapies)

Novel small-molecules with:

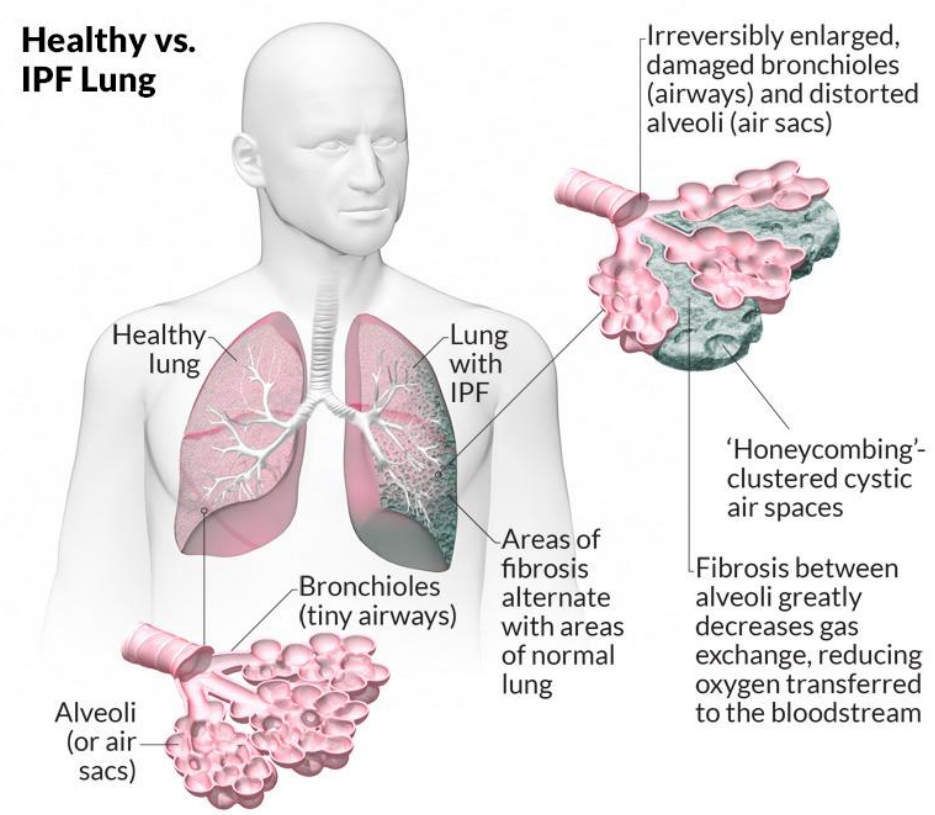
- Superior efficacy/safety
- Novel mechanism(s) of action
- Multi-purpose chemical library

Fibrosis

Fibrous connective tissue deposition in response to Injury
Excessive fibrous connective tissue deposition in response to pathology = Loss of function

- Lung fibrosis or pulmonary fibrosis
- Liver fibrosis
- Kidney fibrosis
- Heart fibrosis
- Skin fibrosis
- Scleroderma or systemic sclerosis
- Cystic fibrosis
- Mediastinal fibrosis
- Bone marrow fibrosis (Myelofibrosis)

Idiopathic Pulmonary Fibrosis (IPF)



Source: Pintrest

IPF Market

- IPF is a progressive, agonizing, debilitating and routinely fatal disease
- Median survival after diagnosis: 3 years - worse than many cancers
- Orphan indication: <200,000 individuals in the United States and ~5 million worldwide
- Mortality rate in US: ~40,000 people/year
- Pirfenidone (Esbriet, 800mg, TID) and Nintedanib (Ovef, 150mg, BID), 2017 annual sales >$1 billion, each
- Only manage to slow, but do not stop or cure IPF
- Unmet medical need: An effective drug with both anti-inflammatory and anti-fibrotic attributes – preferably orally bioavailable
- Potential “Fast-track” regulatory path

Competitive Landscape for IPF

Phase I and II - Ongoing in the clinic:

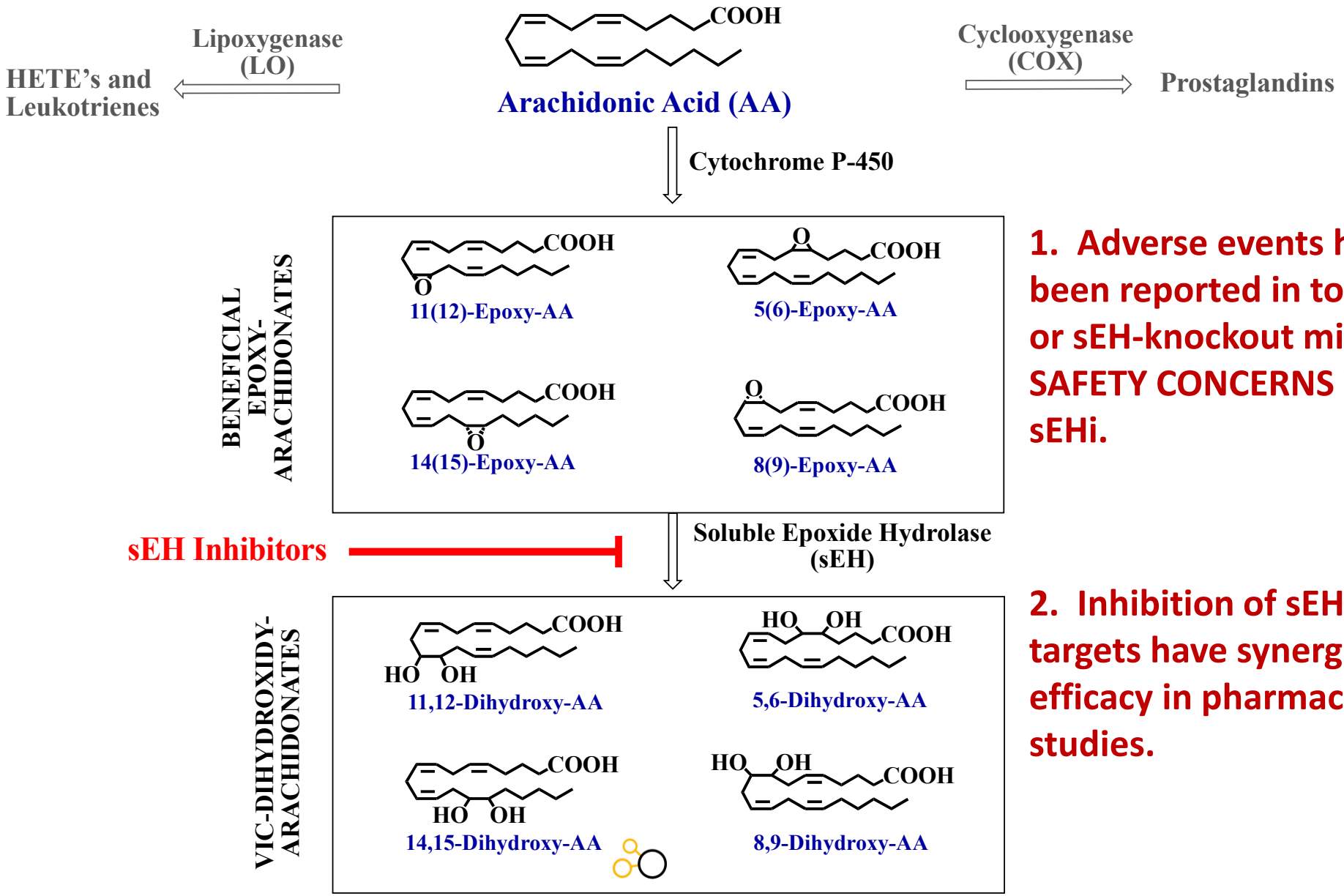
- Pirfenidone and Nintedanib (alone or in combinations)
- Repurposed oncology/virology drugs
- New agents:
  - 2 biologics
  - 2 small molecule kinase inhibitors
  - 1 Integrin inhibitor
  - 2 Leukotriene modulators

Phase III recruiting for 2 new agents in 2018 :

- ART-123 (Asahi-Kasei, thrombomodulin alpha)
- PBI-4050 (Prometic Life Sci)

OROX BioSciences Core Technology

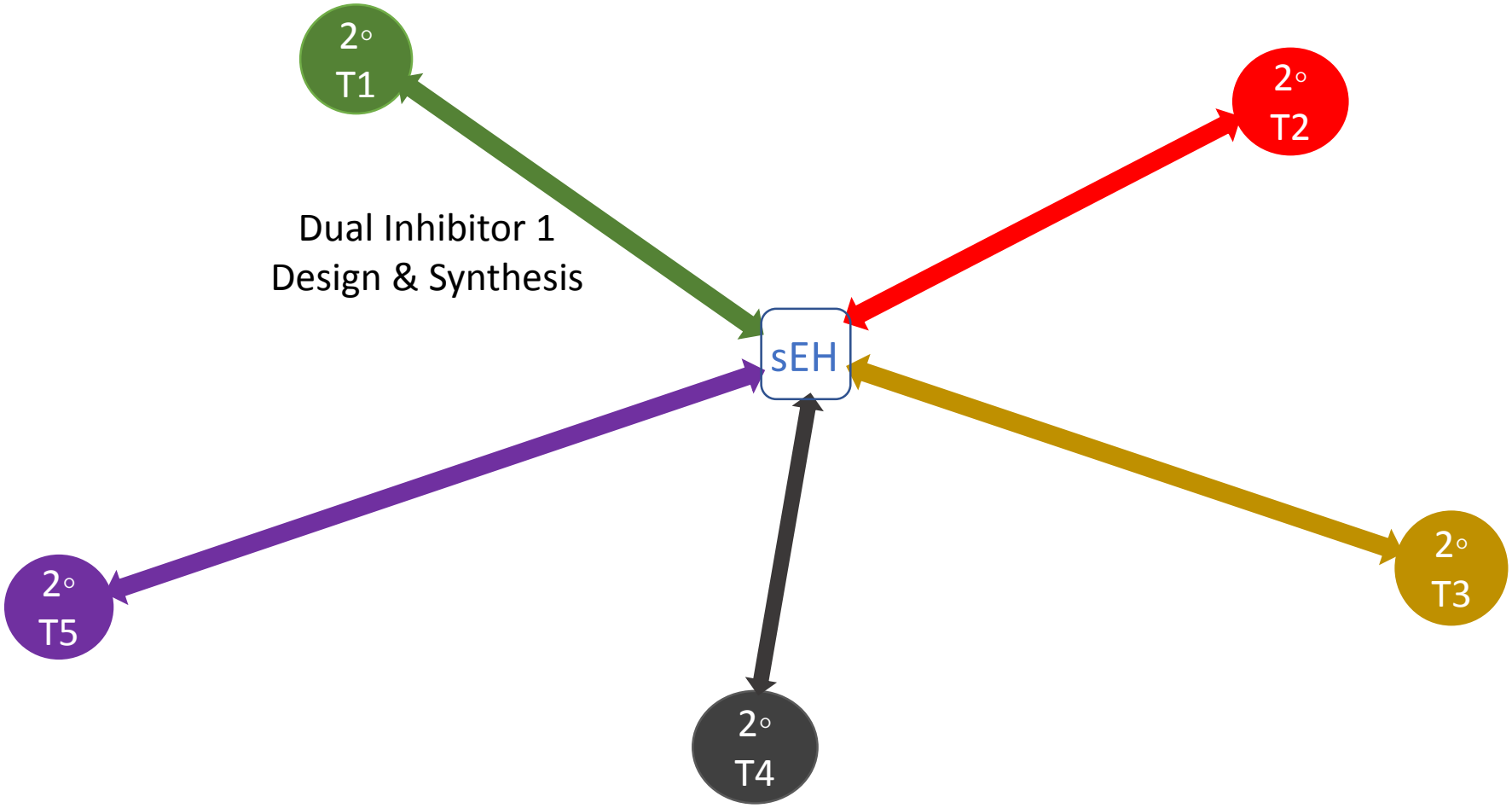
Novel MOA - Modulating Lipid Metabolism



1. Adverse events have not been reported in toxicology or sEH-knockout mice. NO SAFETY CONCERNS WITH sEHi.

2. Inhibition of sEH + other targets have synergized efficacy in pharmacology studies.

Core Technology – Modulating Lipid Metabolism



But does dual inhibition apply to fibrosis?

Proof-of-Concept: sEHi/COXi

Mouse Bleomycin-Induced Lung Fibrosis (Established preclinical Gold Standard)

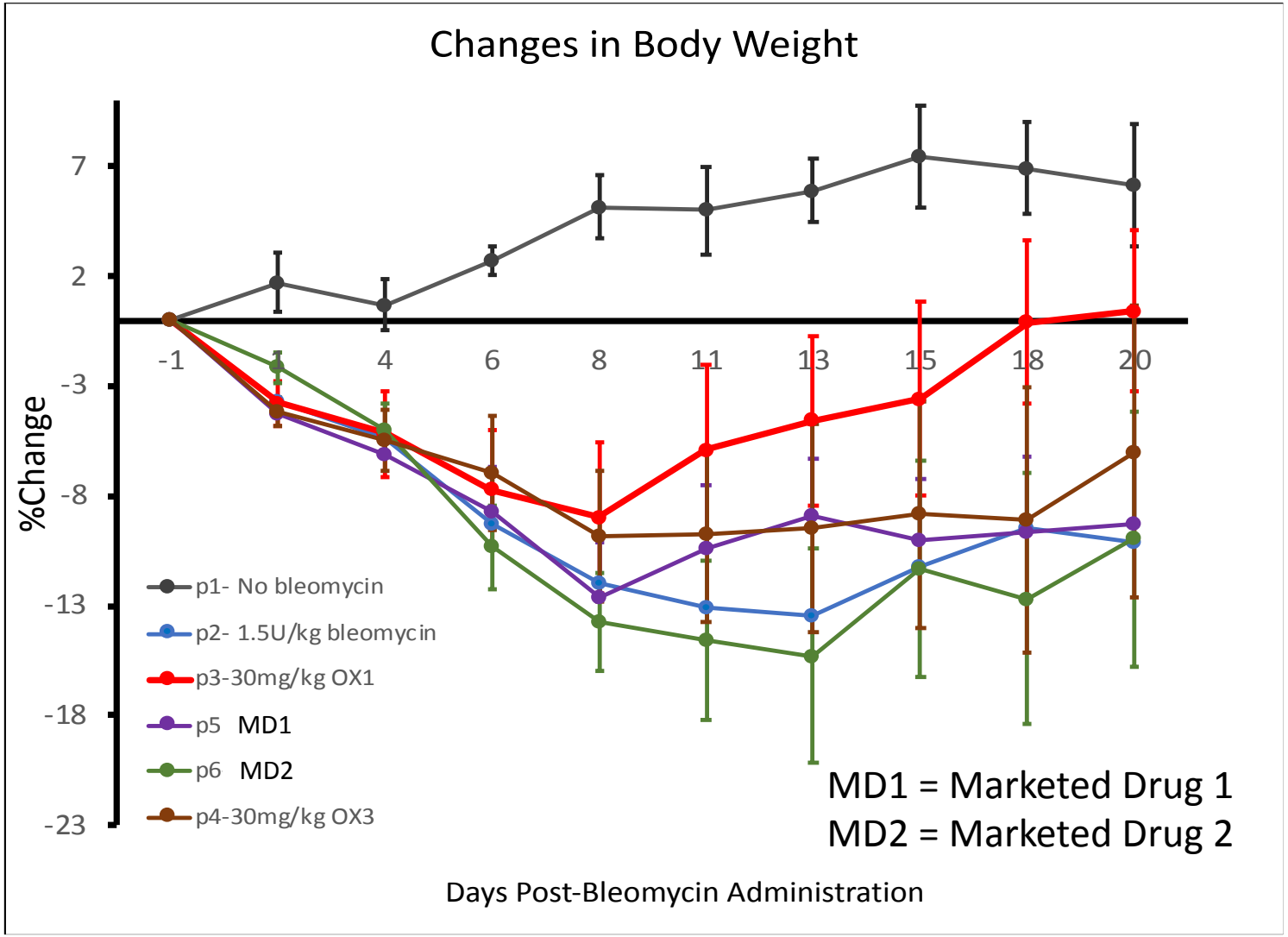
- Questions:

1. How does a sEHi perform vs. marketed drugs?
2. Does a dual sEH inhibitor offer an advantage?

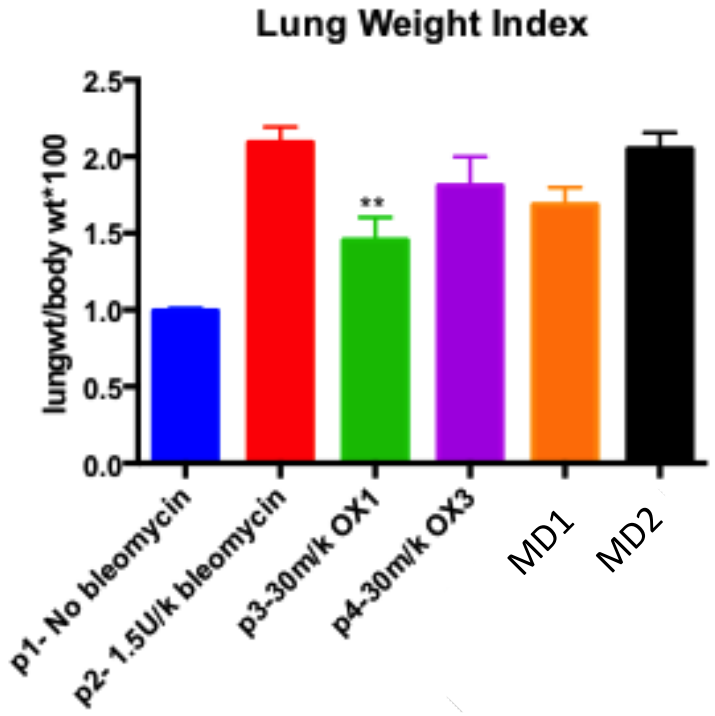
Test articles:

- OX1: Dual inhibitor of sEH + a secondary target
- OX3: Selective inhibitor of sEH
- Pirfenidone
- Nintedanib

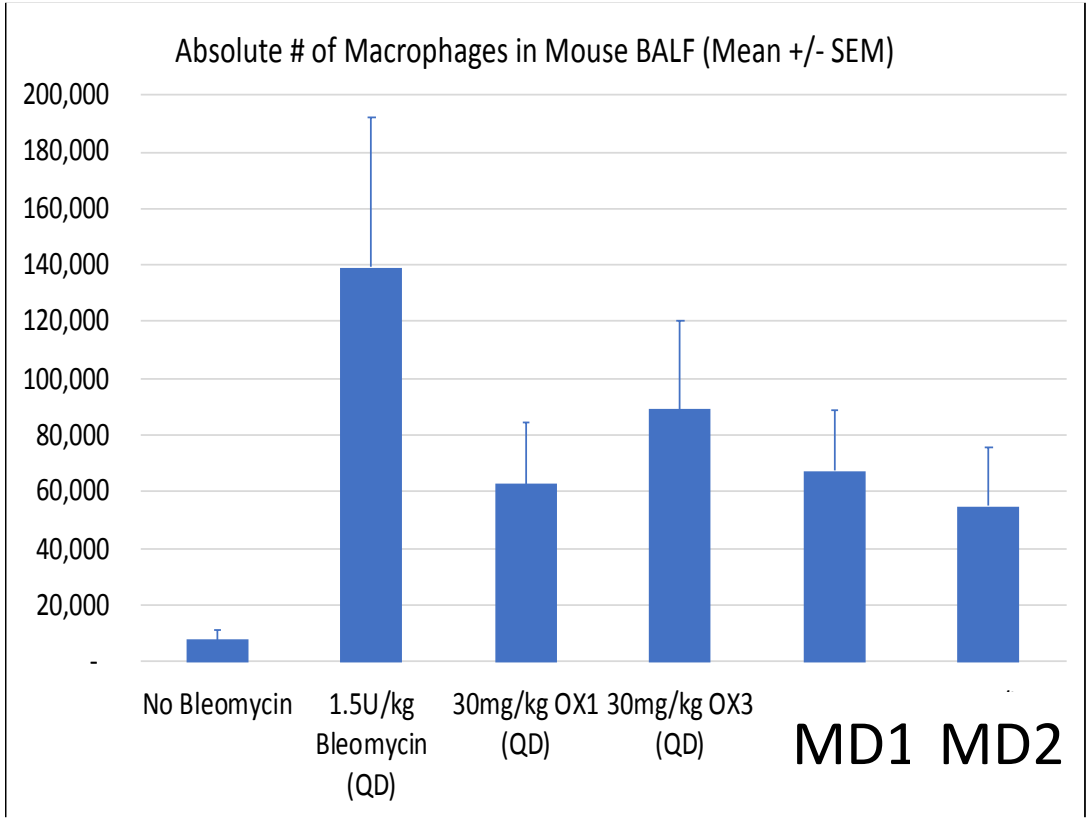
OX1-Treated Animals Experienced A Transient Change in Body Weight

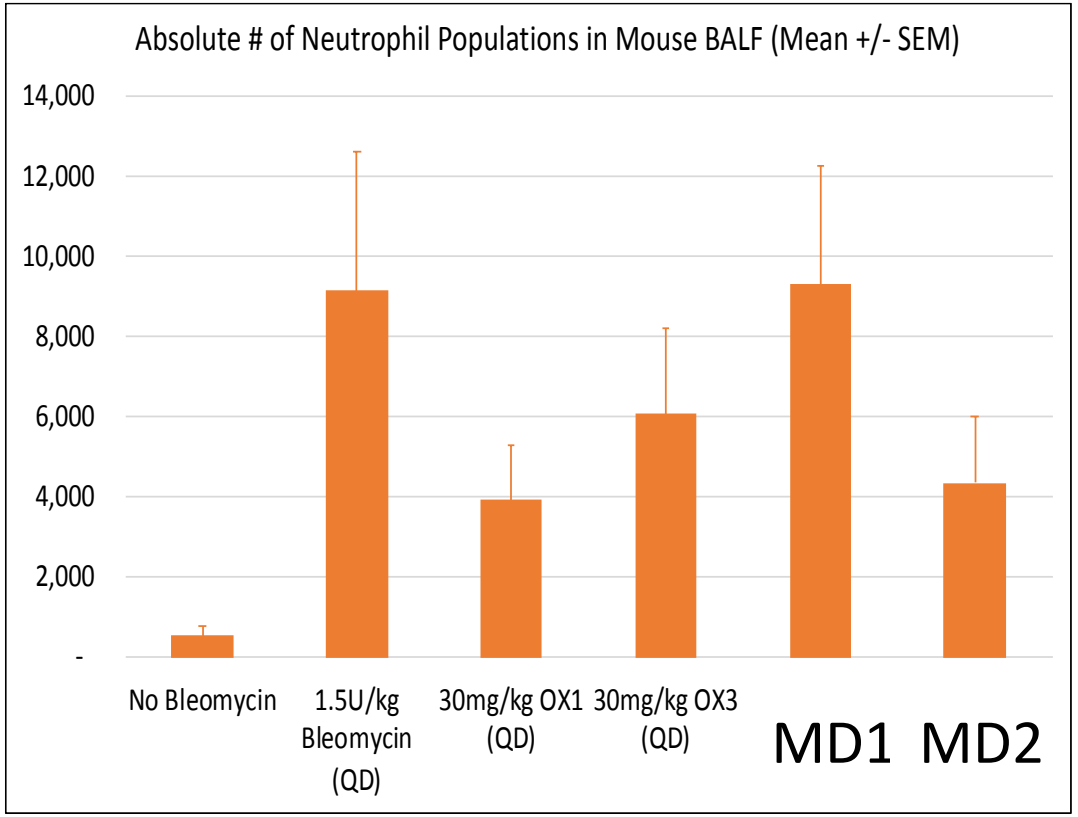


OX1-Treated Animals Exhibited Lower Lung Weights (Less Inflammation/Fluid Accumulation)

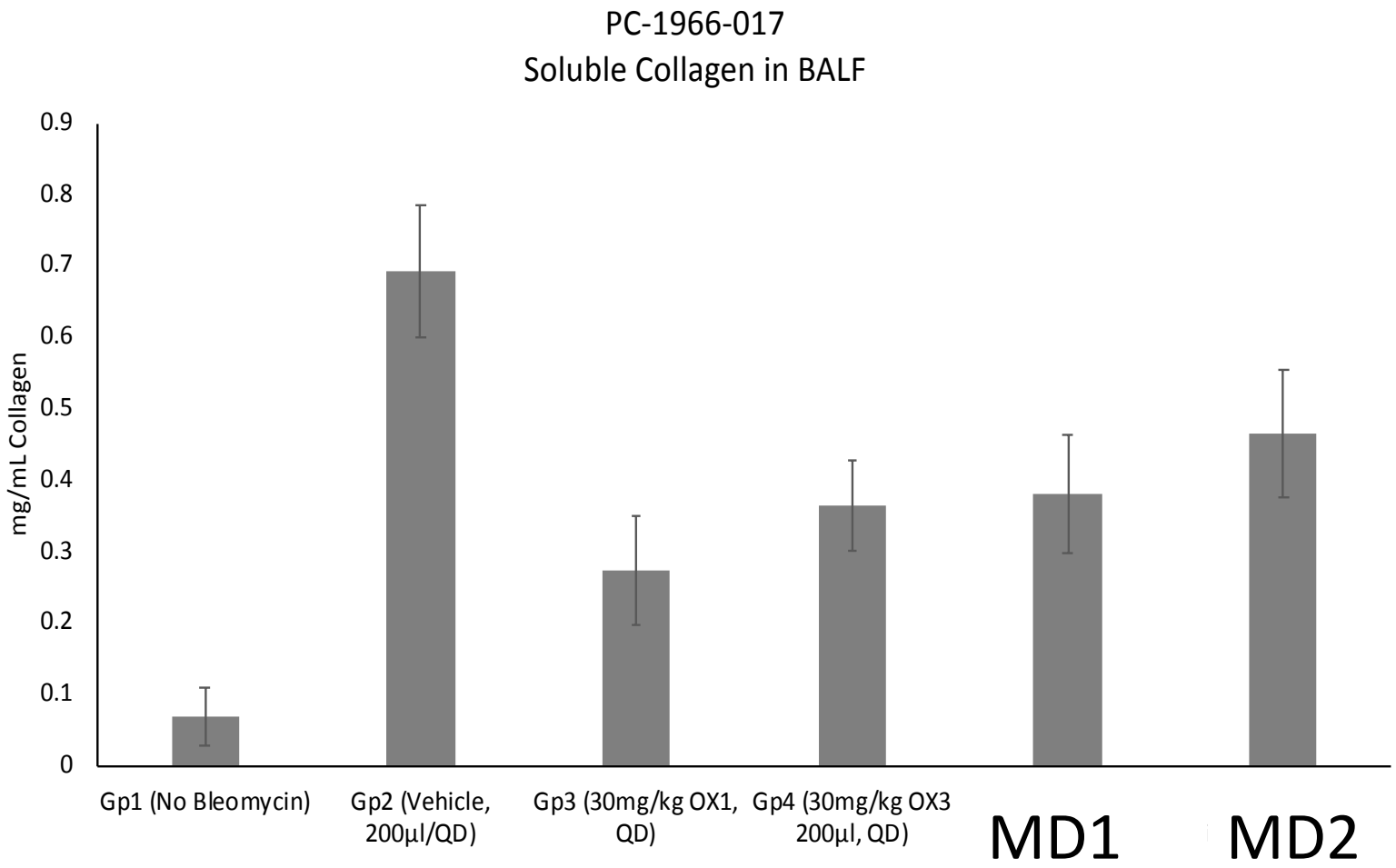


OX1-Treated Animals Exhibited Favorable Bronchoalveolar lung fluid (BALF) Cell Counts



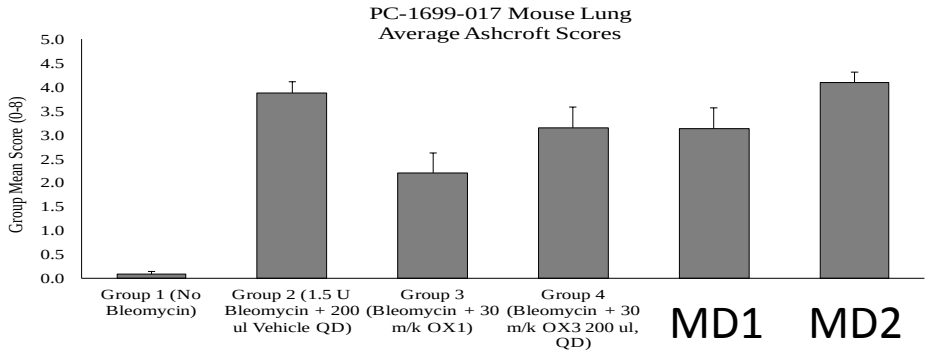


OX1-Treated Animals Exhibited Lower BALF Soluble Collagen Levels (Less Fibrous Connective Tissue)



Every Lung Histology Score Favored OX1-Treated Animals

A.



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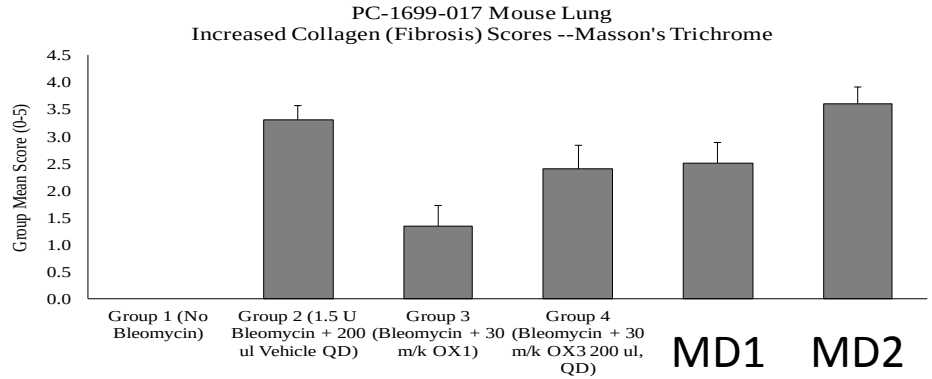

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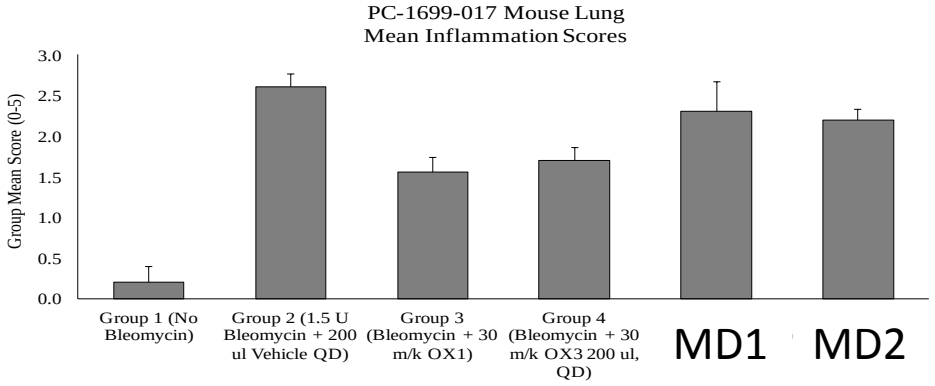

CONCLUSION:

1. OX1 demonstrated superior pre-clinical efficacy vs. marketed IPF therapies
2. Inhibition of a secondary target was beneficial

QUESTION:

If all 4 these were in discovery stage, which would you have advanced into development?

Competitive Advantage

1. Safe target (sEH knock-out mouse and animal/human safety data)
2. Novel and untapped target (great potential)
3. Significantly de-risked (efficacy demonstrated, already in LO stage)
4. Ease of synthesis (Patentable space, 5-7 step synthesis)
5. Secured space (Patent filed)

Strategy

- Parallel approach in discovery:

1. Advance OX1 into preclinical development
2. Design and synthesize superior dual inhibitors (sEH + secondary targets)

- Test NCE for IPF and other fibrotic indications
- Strategic partnership

Seeking

- Strategic alliance with Pharma/Biotech (with interest or expertise and capabilities in fibrosis)
- VC partnership (with previous investments in orphan/fibrosis indications)

THANK YOU!

memo@oroxbios.com
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