Developing Precision Targeted Therapies to Treat Debilitating & Disfiguring Fibrotic Diseases

$2.5M Convertible Note to Fund Key Phase 1B Clinical Study of Lead Drug Product with an Early Exit Possible

Executive Summary

Proprietary Drug Platform to Treat Skin & Lung Fibrosis and Cancer

- Thirona's Precision Targeting **overcomes the safety challenges with TGF-β inhibition**, the master regulator of fibrosis
- Targeting achieved by a combination of FBM5712 (small molecule NCE, with v. short systemic half-life) and unique delivery technology designed to further minimize exposure

Lead Product TBIO-101: IND Activated

- Remarkable preclinical PK/PD & safety profile
- FBM5712 licensed from top-5 pharma
- IND reached with ~$10M in convertible notes from Mannkind and Encube

Initial Focus: Multiple indications with significant unmet need

- **Hypertrophic & keloid scars, scleroderma, squamous cell carcinoma**
  - Multi-$B revenue opportunities

Executive Summary:

A $2.5M Investment Opportunity [via New Convertible Note]

Achieve ‘Clinical Proof-of-Concept’ Key Valuation Inflection Point

- **Phase 1 complete: Drug well tolerated - no significant adverse findings and minimal plasma exposure demonstrated**
- **Phase1B:** Now initiated. Dosing began early December. Goal to demonstrate human safety, selective drug delivery to the skin, inhibition of fibrosis and anti-scarring efficacy.
- **> $1.6M already closed**
- **For the remaining ~$1M, we are now doing rolling closes, on a first come basis**

Open to $5M Equity Plan

Experienced Management Team

- >150 INDs filed
- Deep fibrosis & dermatology drug development expertise
- Involved as Management in more than 10 successful exits (IPOs and/or M&As)

Team with Proven Track Record
> 150 INDs; Multiple Exits; 30+yrs Experience

J. Gordon Foulkes, PhD, Founder & CEO

- Former CSO, OSI (Astellas acq): CTO Aurora (Vertex acq.)
- Managing Director, RiverVest Ventures
- CEO, Excaliard (Pfizer acq.), skin fibrosis focus
- Executive Chair, Redwood Bioscience (Catalent acq.)
- Extensive background in kinases (first purified PTK); discovery of Tarceva (EGFR kinase inhibitor); discovered TGF-β3 (OSI)

David Bullough, PhD, Founder & CSO

- Former CSO, Viking (VKTX)
- Former Executive Director, Pfizer and VP RaNA/Translate (Sanofi)
- VP Preclinical Development, Metabasis
- Expert in small molecule safety, DMPK & drug development

George Mooney, PhD, Founder & EVP Pharm Sciences

- Former VP Exploratory Develop & Pharm. Sciences, Pfizer
- Extensive CMC experience including topical drug formulations

Karen Boezi, COO

- Former CEO, Redwood Bioscience (Catalent acq.)
- Founding Partner, $600M life science venture firm (TMP)
- Investor in >20 companies with successful exits

Charles Ellis, MD, CMO

- Professor Emeritus of Dermatology, University of Michigan
- Over 300 clinical trials
- One of the most cited dermatologists worldwide

Carmen Kerschbaum, MBA, CFO & Director

- Former SVP Finance Pfizer WW R&D & Business Innovation (M&A/Strategy)
- Former SVP Finance & Business Operations (COO) Roche Pharma R&D

Craig Audet, PhD, EVP, Regulatory Affairs

- Former SVP Global Regulatory Affairs, Arena Pharma
- Former VP US Regulatory Affairs, Sanofi-Aventis

Independent Board Members

Nancy Hutson, PhD

- Former SVP R&D, Pfizer

Kay Chandler, JD

- Former Chair of Cooley's Life Sciences Practice & Woman's Initiative

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Clinical & Scientific Advisors

TGF-β

Rosemary Akhurst, PhD
Prof. in Residence,
UCSF Helen Diller Cancer Center

Peter ten Dijke, PhD
Prof. at Leiden Univ. Medical Center

SCLERODERMA

Nunzio Bottini, MD, PhD
Director of Kao Autoimmunity Institute,
Cedars Sinai LA

Christopher Denton, PhD, FRCP
Prof. of Experimental Rheumatology, UCL
Head of largest UK Scleroderma Center

Robert Lafyatis, MD
Prof. of Medicine, Rheumatology &
Immunology, Univ Pittsburgh

CANCER

Steven Bender, PhD
Former Exec. Director Cancer,
Novartis & Pfizer

Art Krieg, MD
Co-founder, CSO, Coley Pharma (Pfizer acq.)
& Checkmate Pharma (Regeneron acq.)

Justin Moser, MD
Medical Oncologist Cutaneous Cancer
Honor Health Res. Inst

Vishal Patel, MD
Cutaneous Oncology Director, GW Cancer Center
Director Dermatology Surgery, GW

FIBROSIS & LUNG DISEASE

Paul Atkins, PhD
Former CEO, Oriel Therapeutics (Sandoz acq.)
Nobel Laureate

Jayne E. Hastedt, PhD
Managing Director, JDP Pharma & Co-lead developing (iBCS) inhaled drugs. Former companies incl. ALZA (J&J acq.), Nektar, GSK, BI

Toby Maher, MD, PhD
Prof. of Clinical Medicine, USC

Paul Wolters, MD
Prof. of Medicine & Director,
UCSF Interstitial Lung Disease Program

DERMATOLOGY, SCARS & PLASTIC SURGERY

Brian Berman MD, PhD
Past VP AAD & President, ADA
Emeritus Prof Derm. U. Miami

Jay Birnbaum, PhD
Past Head of Derm, Novartis
CMO Kythera
Head of Skin Care Wyeth

Mark Jewell, MD
Past President ASAPS
Director of ISAPS

Lamont Jones, MD
Assoc. CMO, Facial Plastic Surgery
Henry Ford Health
Prof Surgery Michigan Univ

Leroy Young, MD
Past Prof. Plastic Surg. WashU
Past President of ASERF

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Fibrotic Diseases:
Multiple Large Indications But Very Few Drugs

1 **Tissue injury, insult or disease**

2 **Healing process goes awry;**
Aberrant TGF-β regulation;
Exaggerated healing response

Excessive accumulation of fibrous connective tissue - Including collagens

3 **Results in formation of thick/stiff/scarred tissue & organ damage**

FIBROSIS

4

TGF- β driving fibrosis now documented in > 20,000 Publications

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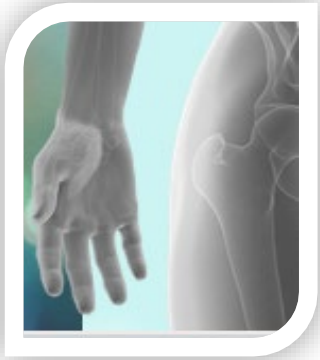
The Solution: Precision anti-TGF-β Platform Multiple Products to Treat Multiple Fibrotic Diseases

Precision Targeted

Skin & Hand



TBIO-101 Dermal

Initial Indications

- **Keloid & Hypertrophic Scars**
- **Hand Disability in Systemic Sclerosis**
- **Cutaneous Squamous Cell Carcinoma**

Additional Indications

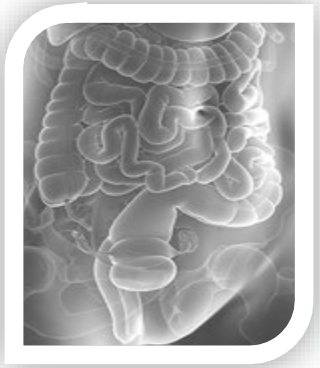
- **Focal Fat Reduction**
- Cutaneous Lupus
- Cutaneous Neurofibromas

Lung

TBIO-201 Inhaled

Indications

- Idiopathic Pulmonary Fibrosis (IPF)
- Interstitial Lung Disease in Systemic Sclerosis (SSc-ILD)



TBIO-301 Internal Organ-Restricted

Indications

- Disclosed under CDA

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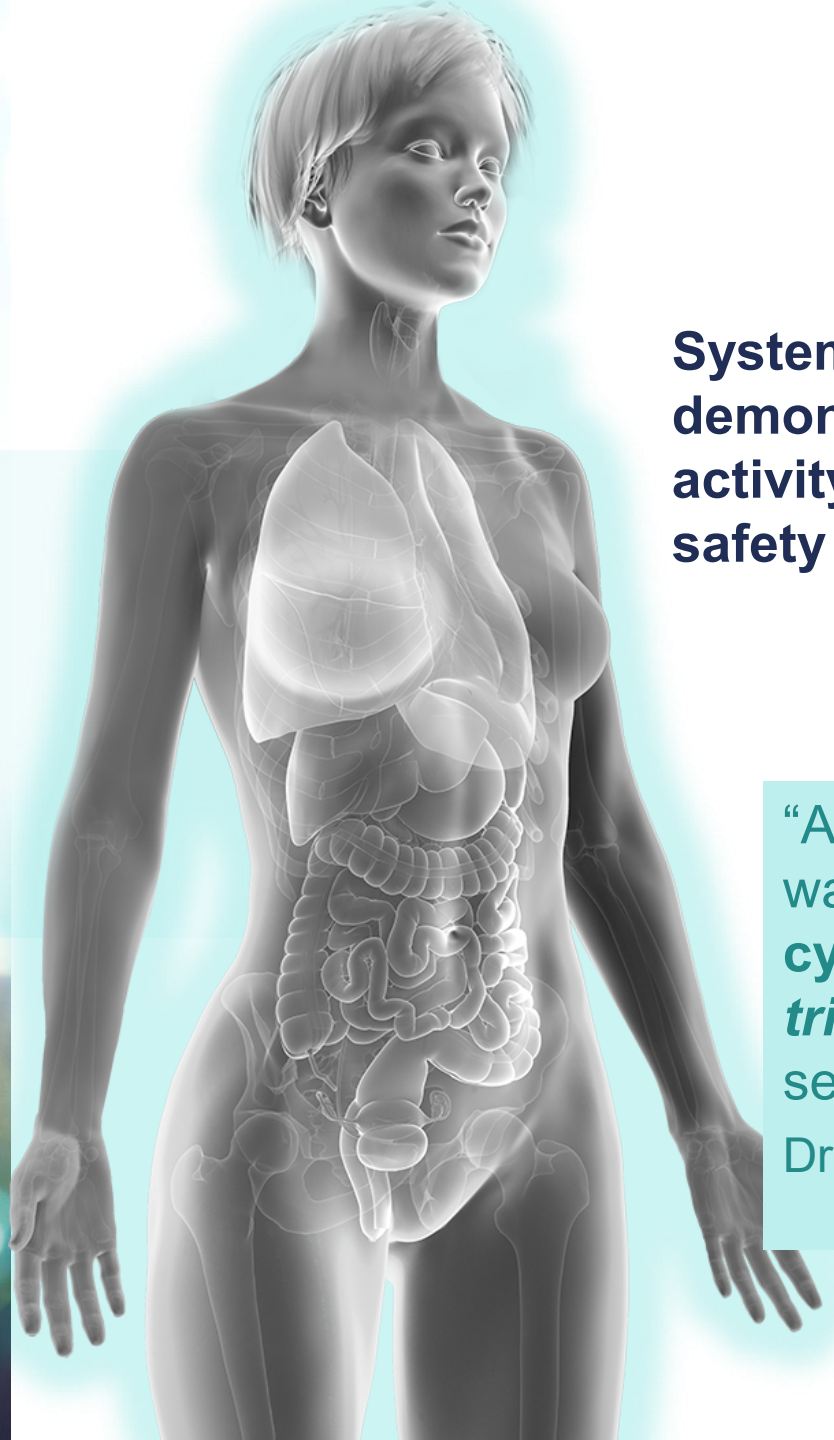
The Challenge: Is Safe Inhibition Possible? TGF-β has Multiple Physiological Roles

- Cardiac valve repair
- Wound repair
- Bone repair
- Immune modulation etc.



Systemic TGF-β Inhibitors demonstrate anti-fibrotic activity but unacceptable safety margins

"As a longtime vet of the TGF-β wars, .. it's **the greatest of the cytokines but an *insidiously tricky bugger*** to target with selectivity"

Dr. M. Gilman, Former SVP Biogen

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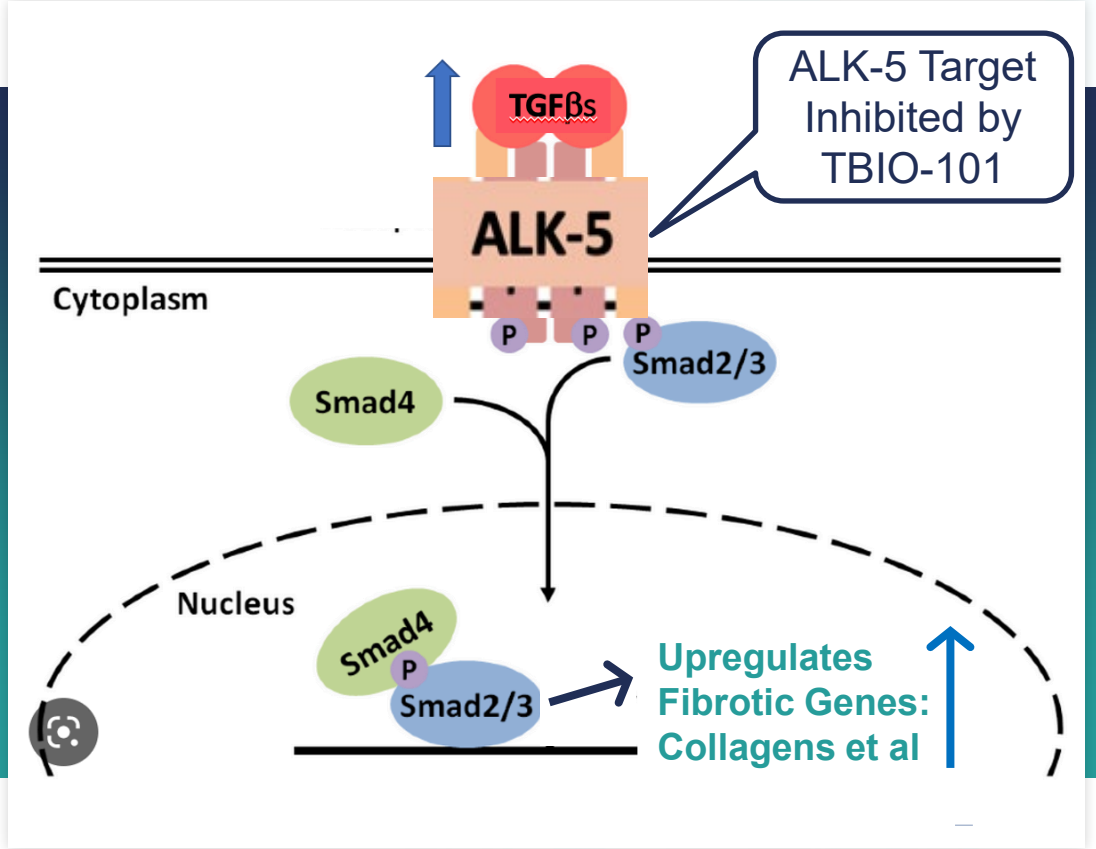
TGF-β: Validated Target as the Master Regulator of Fibrotic Diseases But can Safe Inhibition be Achieved?

- TGF-βs signal through a receptor kinase, ALK-5
- TBIO Products inhibit ALK-5, blocking signaling
- TGF-β role in fibrosis studied extensively (>20,000 publications)



ALK-5 Inhibition → ↓ Collagen Production AND ↑ Collagen Degradation → Reversal of Fibrosis

Aashaq, 2021; Cui, 2019

TBIO-101:
Thirona's Precision Targeting Achieves Optimal Efficacy & Safety

1 **Novel Anti-Fibrotic Therapeutic**

Small molecule FBM5712

- **Potent & selective pan inhibitor** of TGF-βs (1,2,3) thru ALK-5 inhibition
- **Designed for safety:** rapid drug clearance in liver with systemic half-life ≤ 1-2 hours
- Nominated for development by top 5 pharma

2 **Dermal-Selective Delivery Technology**

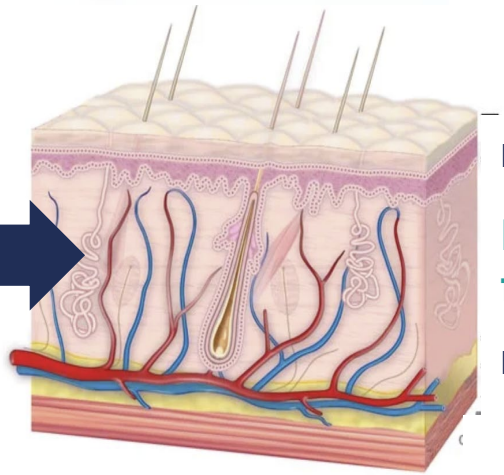
- **Achieves high dermal concentrations** for efficacy
- **Minimizes systemic exposure** for safety

3 **Strong IP & Regulatory Protection**

Dermal Delivery Extensively Optimized

>100 candidates evaluated

High Dermal Concentration Achieved



Minimal Systemic Exposure, Rapid Metabolism

Maximizes Therapeutic Index

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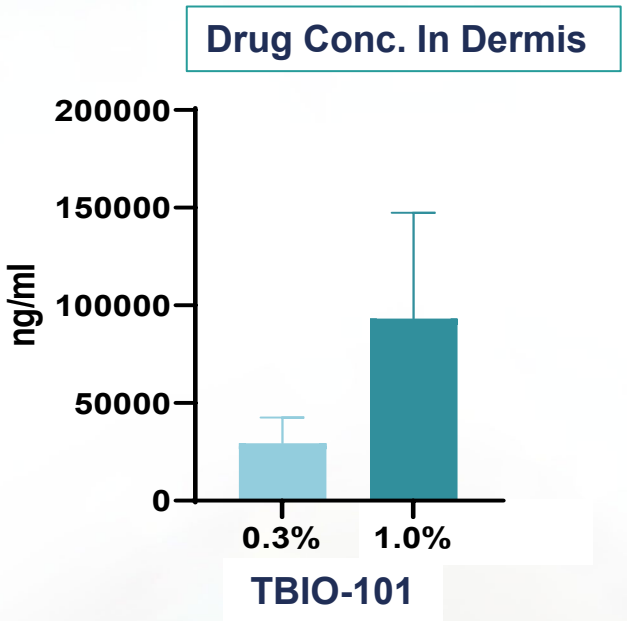
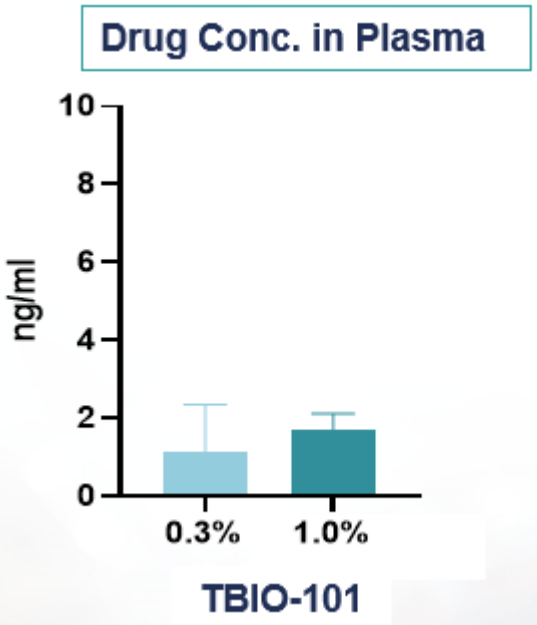
TBIO-101 Achieves Extraordinary Targeted Drug Delivery to Dermis *In Vivo**

- **Target Engagement: >1,000-fold concentration of drug in the dermis** than required to inhibit the TGF-β kinase in human dermal fibroblasts
- **Highly Selective Dermal Delivery: >50,000-fold concentration of drug in dermis vs. plasma**





- **No adverse findings in GLP toxicology studies: IND activated by the FDA**

*Minipigs dosed for 28 days: FDA species of choice for dermal products due to similarity to human skin

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Excellent Preclinical Safety Profile

28-day **TOPICAL** GLP Minipig Study

- **No toxicity at** highest dose of TBIO-101 (1%)

→ **No dermal toxicity observed**

→ **No systemic toxicity observed**

28-day **ORAL** GLP Rat Study

- **No toxicity at** highest dose of FBM5712 (300 mg/kg)
- >10,000x systemic exposure projected in Phase 1

→ **No systemic toxicity observed**

IND activated by FDA

→ Safety Margins so high FDA approved first in human dosing at the highest concentration

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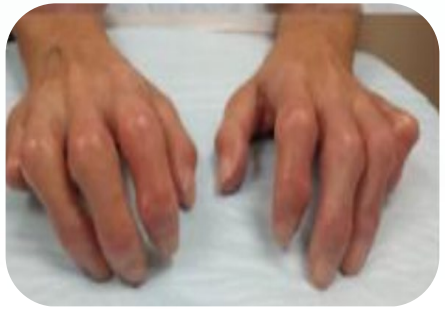
TBIO-101: Multiple Indications with Est US Peak Sales >$4 Billion

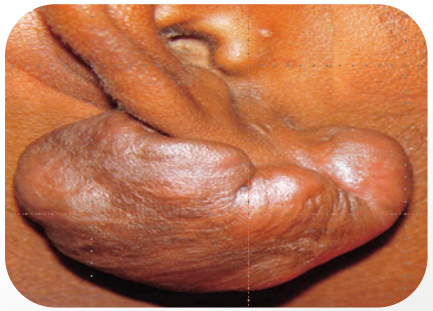
Hypertrophic Skin Scars

- High prevalence in surgery, cosmetic disfigurement
  - 51% sternotomies, 26% C-sections, etc.
- No effective drugs
- **Estimated Peak US Sales: >$2.5B/yr (self-pay mkt)**



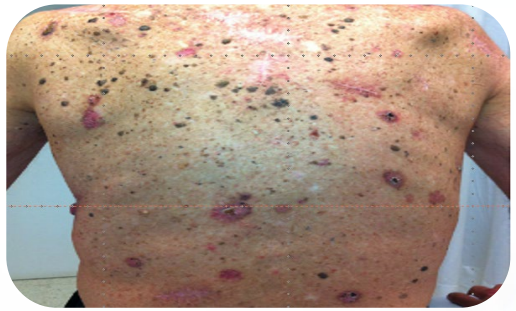
Scleroderma in Systemic Sclerosis

- Orphan disease; 80% women
- > 100K U.S. patients; > 90% with skin fibrosis, > 40% severe hand impairment
- No approved drugs
- **Estimated Peak US Sales: ~$1B/yr**



Keloids

- Disfiguring, itchy & painful tumor-like scars
- Prevalent, especially in people of color (4-16%)
- Surgical revision but regrowth (40-70% cases)
- No approved drugs
- **Estimated Peak US Sales: >$700M/yr**



Cutaneous Squamous Cell Carcinoma

- ~1.4M early & late stage U.S. cases/yr
- Early: surgery not optimal for multiple lesions, cosmetic issues; no approved drugs
- Late (5%) not effectively treated; ~2x more deaths/yr than melanoma
- **Estimated Peak US Sales: >$500M/yr**

Clinical Validation for Key Role of TGF-β in Scleroderma

Study of Fresolimumab*
Sanofi's IV pan-TGF-β antibody

- **TGF-β skin fibrosis** biomarkers* and **mRSS**** significantly reduced as early as 3 weeks
- **REVERSAL** of skin fibrosis
  - Median decline of "-9.5" on mRSS**, p=0.0024 at week 17
- However, **anemia and bleeding complications** were observed

No drug has ever achieved this magnitude of rapid mRSS decline

Implications for TBIO-101:

- Also inhibits all 3 TGF-βs from signaling
- Potential for clinical benefit **without side effects of systemic TGF-β inhibition**

**mRSS = modified Rodnan skin score for skin thickness/fibrosis:
A decline of 5 or more considered clinically meaningful

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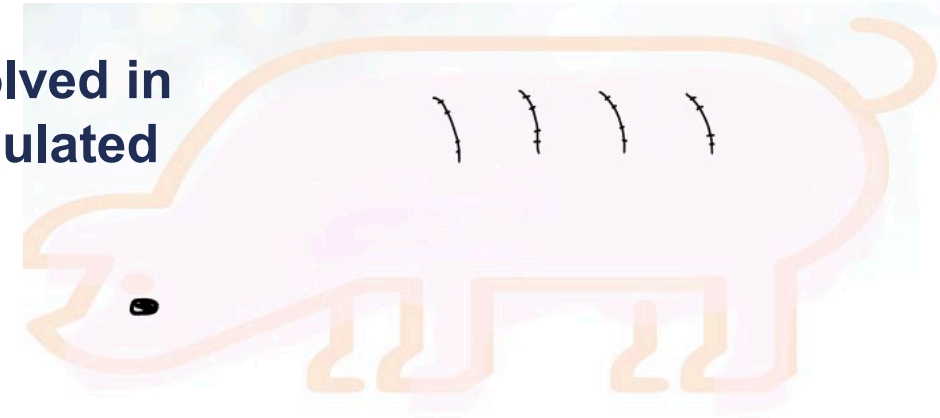
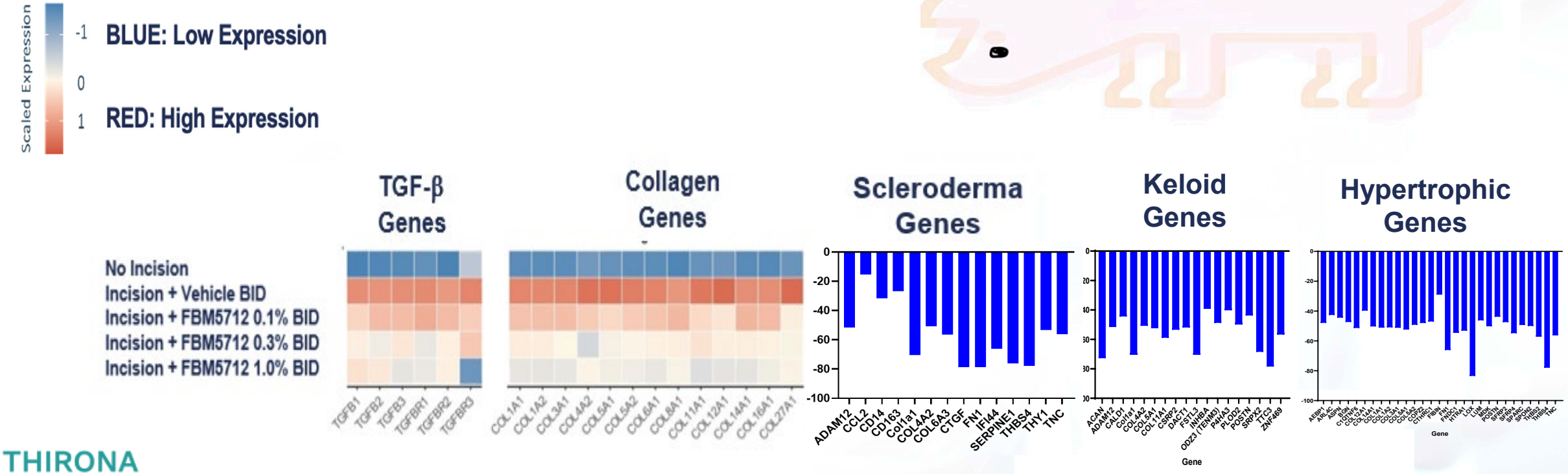
TBIO-101:
Inhibits Surgically-Induced Dermal Fibrosis Minipig Model

- **TBIO-101 inhibits expression of fibrotic genes *in vivo***

- **Expression of TGF-βs, collagens & the key genes involved in scleroderma, keloids and hypertrophic scars downregulated**





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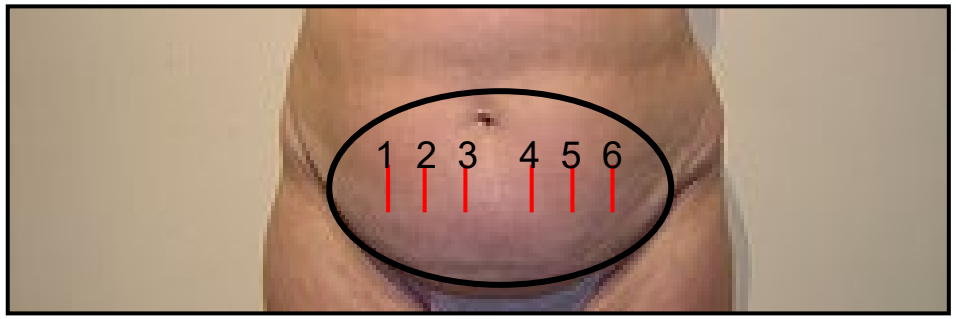
TBIO-101 Phase 1B Part A (Study FBM5712-102)

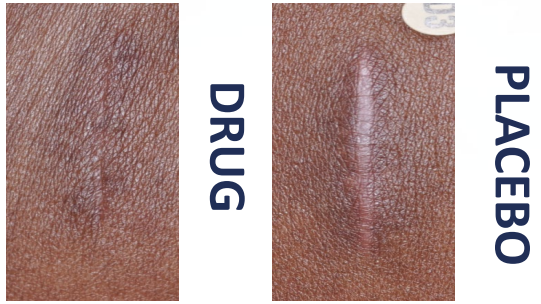
Part A: Safety & PK Study with FBM5712 1% (N=5). **Now completed.**

- Design: Subjects eligible for an abdominoplasty study
  - One day BID drug doses to abdominal skin
  - Seven day “wash out” period
  - Same subjects then re-dosed for 7 days BID
- **Safety:**
  - **No local (skin) tolerability issues**
  - **No clinical safety concerns**
  - **No clinical laboratory concerns (chemistry, hematology, urinalysis)**
- **PK:**
  - **Low plasma drug levels ~ 0.3ng/ml [≤ to levels in minipigs] and reaching steady state in < 7 days**
  - **Critically, these very low plasma levels of TBIO-101 predict no systemic drug safety concerns**

TBIO-101 Phase 1B Anti-Scarring Study (FBM5712-102)

- **Phase1B: Trial Now Initiated. POM & POC Study with FBM5712 1%** (N=10)
  - Objectives: Demonstrate TBIO-101 is safe and well tolerated with low systemic drug levels, inhibits dermal fibrosis; prevents hypertrophic scarring (precursor to multiple Ph2s)
  - Subjects will be dosed for 28 days BID. **Dosing in the First Cohort started early December**





- **Within patient design** i.e., drug v placebo comparison in the same subject e.g.,TBIO-101 applied to Incisions 1-3 : Placebo Vehicle Gel to Incisions 4-6: Multiple biopsies to measure profibrotic gene expression. Equivalent to a 60-person conventional design combined with better statistics.
  - At study-end, patients provided a free abdominoplasty (typically cost > $18K), removing all excess skin as illustrated by the black oval area above

Raising $2.5M Note & Exit or Close $35M Series A:
Capital Efficient Spend to Value-driving Milestones

IND reached by $10M Notes from Mannkind & Encube Ethicals

TBIO-101

Exit, Partnership or Series A

Series A Exit Possible Yr 3

POM/ POC → **POC**

Phase 1 SD / 7-day MD + 28-day incisional fibrosis study

Phase 2A 28-day studies in keloid & hypertrophic scars; scleroderma; cutaneous squamous cell carcinoma

3-month non-clinical GLP tox

New $2.5M Note

$30M

Open to $5M Equity Plan to Enable 3 Month Tox & longer Ph2s

IND Candidate

TBIO-201

$5M

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Other Biotech Companies with a Targeted ALK5i Program

AgomAb Therapeutics

Focused on ALK5i organ-restricted inhibition

- **No dermal product**
  - Lead product for fibrostenosing Crohn's disease (Ph 2)
  - Lung-restricted product for IPF (Ph 1)
    - > **Nebulized formulation – not ideal for all patients**
- Different clearance mechanism
- Based in Belgium
- Raised $325M to date, ALK-5is only clinical-stage products

Enveda Biosciences

Engineering new natural products-based drugs utilizing machine learning

- ALK5i is 7th program of 12 in pipeline
  - Gut-restricted fibrostenosing Crohn's product pre-IND studies
  - **Dermatology product but local injectable and pre-IND studies**
    - > **Significantly behind Thirona**
  - Lung product (inhaled) in lead selection phase
- Raised $360M to date to fund programs against 12 different targets

Potential Pharma Partners & Acquirors: Companies in Four Broad Areas

TGF-β/Fibrosis

- abbvie
- AstraZeneca
- AMGEN
- Boehringer Ingelheim
- Bristol Myers Squibb
- CSL Behring Biotherapies for Life™
- GSK
- MERCK
- NOVARTIS
- Roche

Dermatology

- abbvie
- almirall feel the science
- AMGEN
- BAUSCH Health
- GALDERMA
- GSK
- Incyte
- JT
- Johnson & Johnson
- LEO
- Lilly
- maruho
- Pfizer
- REGENERON

Orphan Diseases

- ALEXION AstraZeneca Rare Disease
- AMGEN
- Bristol Myers Squibb
- Johnson & Johnson
- NOVARTIS
- Pfizer
- Roche
- sanofi
- Takeda

Immuno-Oncology

- AstraZeneca
- Bristol Myers Squibb
- GSK
- Incyte
- MERCK
- MERCK SERONO
- ono
- Pfizer
- REGENERON
- Roche

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Comparables: Significant Value Created

11/5 Valuation

Public

BICARA THERAPEUTICS™
(1)(2) **$1.3B**

KEROS THERAPEUTICS
(4) **$2.5B**

PLIANT
(1)(2) **$955M**

ScholarRock
(1)(2) **$2.8B**

IPO + M&A

ACCELERON
(1)(4) **Merck $11.5B**

Prometheus Biosciences
(3) **Merck $10.8B**

INTERMUNE®
(2) **Roche $8.3B**

M&A

amira pharmaceuticals
(2)(3) **BMS** Up to **$475M**

EXCALIARD PHARMACEUTICALS, INC.
(2)(3) **Pfizer >$100M upfront alone**

Promedior
(3) **Roche** Up to **$1.4B**

Tilos THERAPEUTICS
(1)(2) **Merck Up to $773M**

(1) Product(s) with TGF-β/integrin selective systemic inhibition
(2) Product reduces TGF-β or is in TGF-β pathway
(3) Focused on Thirona indication(s) with different target
(4) Focused on inhibiting other pathways in TGF-β superfamily to address different diseases

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Thirona Bio: Compelling Investment Opportunity

- **Precision Targeted Anti-fibrosis Platform**
  - Addresses historical therapeutic index challenges with TGF-β inhibition, a high value drug development target
  - TGF-β recognized as master regulator of fibrosis
- **Multiple, disfiguring & debilitating fibrotic conditions**
  - Profound unmet medical needs, huge market potential
- **Clinic-ready lead product, TBIO-101**
  - TBIO-101 has remarkable safety, precision targeting, and efficacy in preclinical studies
  - Clinical proof-of-mechanism and efficacy within 12 months
- **Strong IP & regulatory protection**
- **Pharma investment & licensing interest**
- **Experienced management team**
  - Proven track record in drug development, financings & exits

THIRONA BIO

Developing Precision Targeted Therapies to Treat Multiple Debilitating & Disfiguring Fibrotic Diseases

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