IKAIKA Therapeutics

First-in-class Anti-Fibrotic Biologics

Advancing therapies designed from genetic signals

Science Contact:
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JUNE 2025| NON-CONFIDENTIAL CORPORATE DECK

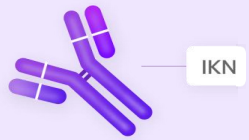
Uncovering a novel target, **LTBP4**, capable of modifying the outcome of fibrotic diseases.

Our ask

- **Series A fundraising of $15M** to reach first in human (FIH)

About Ikaika

- **Preclinical** stage private company (C-Corp)
- First-in-class anti-fibrotic biologics



Fibrosuppresant

mAb Therapy for a Novel Fibrosis Target LTBP4

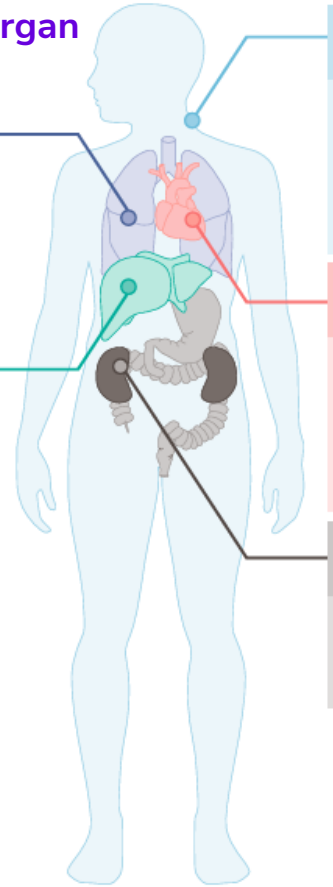
- **Genetic signals** identified novel target that regulate muscle disease progression, including muscular dystrophy

Why now

- **Gap in SOC** of treatments in fibrotic diseases
- Extensive non-dilutive capital with the first **NIH NINDS Blueprint award** for a biologic (PIs: Demonbreun / McNally)
- Robust **IP portfolio** including issued patents US9,873,739B2; and recent application for composition of matter 63/764,259

Targeting fibrosis: A medical condition associated with many chronic diseases

Fibrosis prevalence per organ



Lung
1:1,500
- Idiopathic pulmonary fibrosis
- Interstitial lung disease
- Cystic fibrosis

Liver
1:4
- Hepatitis B or hepatitis C
- Long-term alcohol abuse
- Non-alcoholic steatohepatitis
- Non-alcoholic fatty liver disease
- Cholestasis
- Autoimmune hepatitis
- Cirrhosis

Skin or systemic
1:5,400
- Scleroderma
- Keloids
- Hypertrophic scars
- Graft-versus-host disease
- Radiation

Heart
1:60
- Myocardial infarction
- Hypertension
- Aortic stenosis
- Hypertrophic cardiomyopathy
- Heart failure

Kidney
1:6
- Chronic kidney disease
- End-stage renal disease
- Renal interstitial fibrosis

Image reference in notes

Potential impact of our pipeline of mAbs

- Fibrosis is the abnormal deposition of extracellular matrix (ECM), characterized by pathological tissue scarring impacting organ function
- It is a chronic and progressive medical condition that can lead to organ dysfunction, morbidity and death
- Fibrosis **burden significant**, affecting 1 in 4 people globally
- **Incidence** of major fibrosis-related conditions ~1 in 20

There are currently no therapies that can prevent or reverse fibrosis!

Targeting metabolic dysregulation for fibrosis therapy

Fibrosis impacts rare pediatric diseases like **Duchenne Muscular Dystrophy (DMD)**

Indication overview

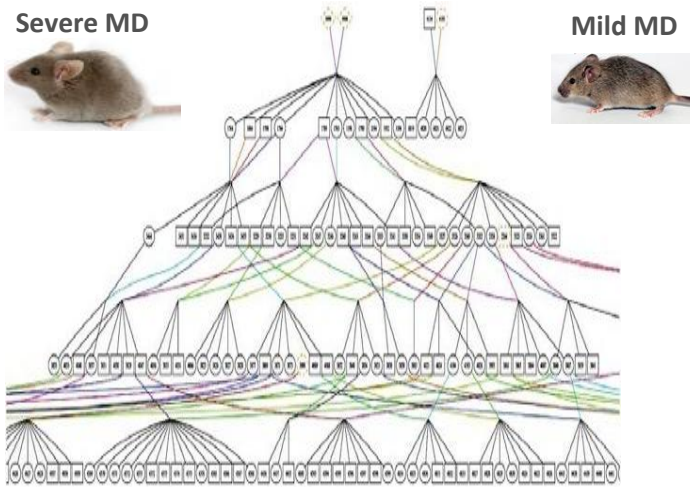
- Progressive **fibrotic, muscle wasting** disorder
- Affects **1 in ~5,000 boys**
- DMD morbidity due to **cardiopulmonary failure**, with poor quality of life (QoL) from an early age
- Devastating progressive disease with an estimated **survival of 35 years**

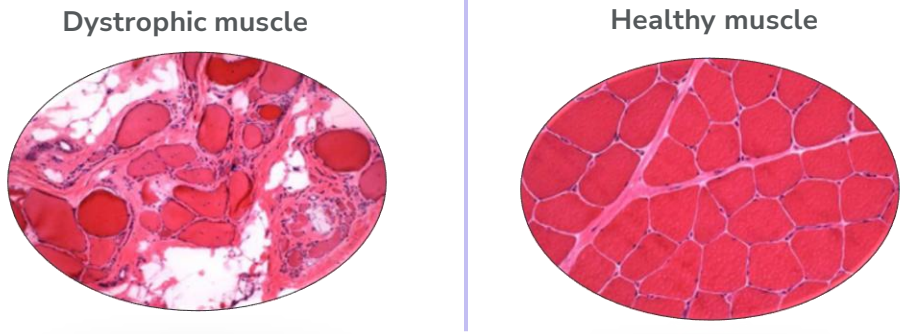
Unmet Needs

- **No effective cure for DMD**
- **Gap in Standard of Care (SOC)** for DMD today: includes chronic steroids associated with many negative side effects
- **Genetic correction therapies target unique disease mutations**, are very costly and plagued with under-performance (e.g. exon skipping)
- **Micro-dystrophin gene replacement therapy** is only partially effective, leaving significant residual fibrosis similar to Becker Muscular Dystrophy, a target indication.
- Need for **mutation agnostic therapies** across all MD types

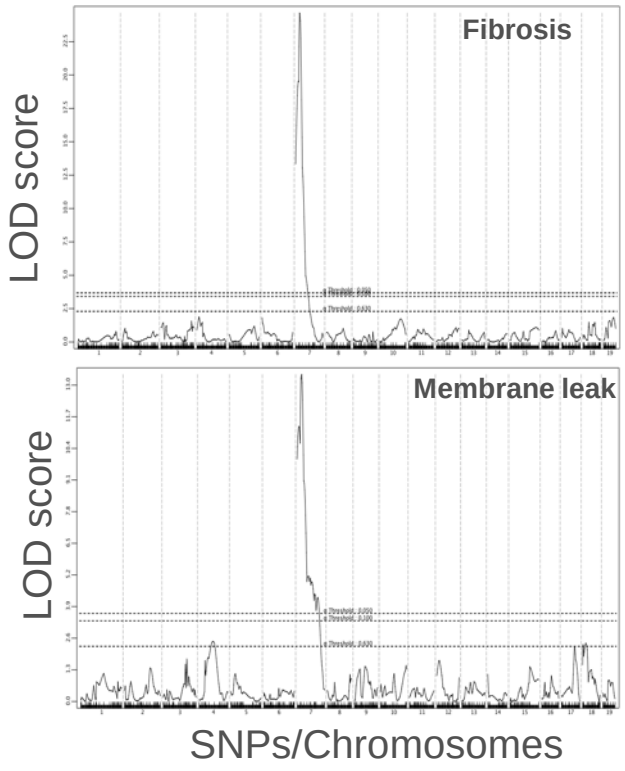
Wijsenbeek, J. et al. N Engl J Med 2020

Genetic signals identified LTBP4 as **modifier of fibrosis** and membrane leak





Region contains **LTBP4**

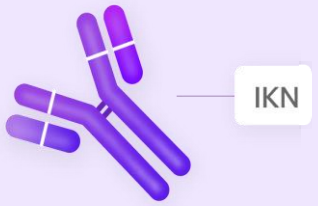


Full length LTBP4

- ✓ **LTBP4** gene highest impact modifier
- ✓ Genetic studies demonstrated LTBP4 mechanism of action driven by **hinge** region
- ✓ **Reduced cleavage** of LTBP4 hinge correlated with **less fibrosis** and milder muscle disease

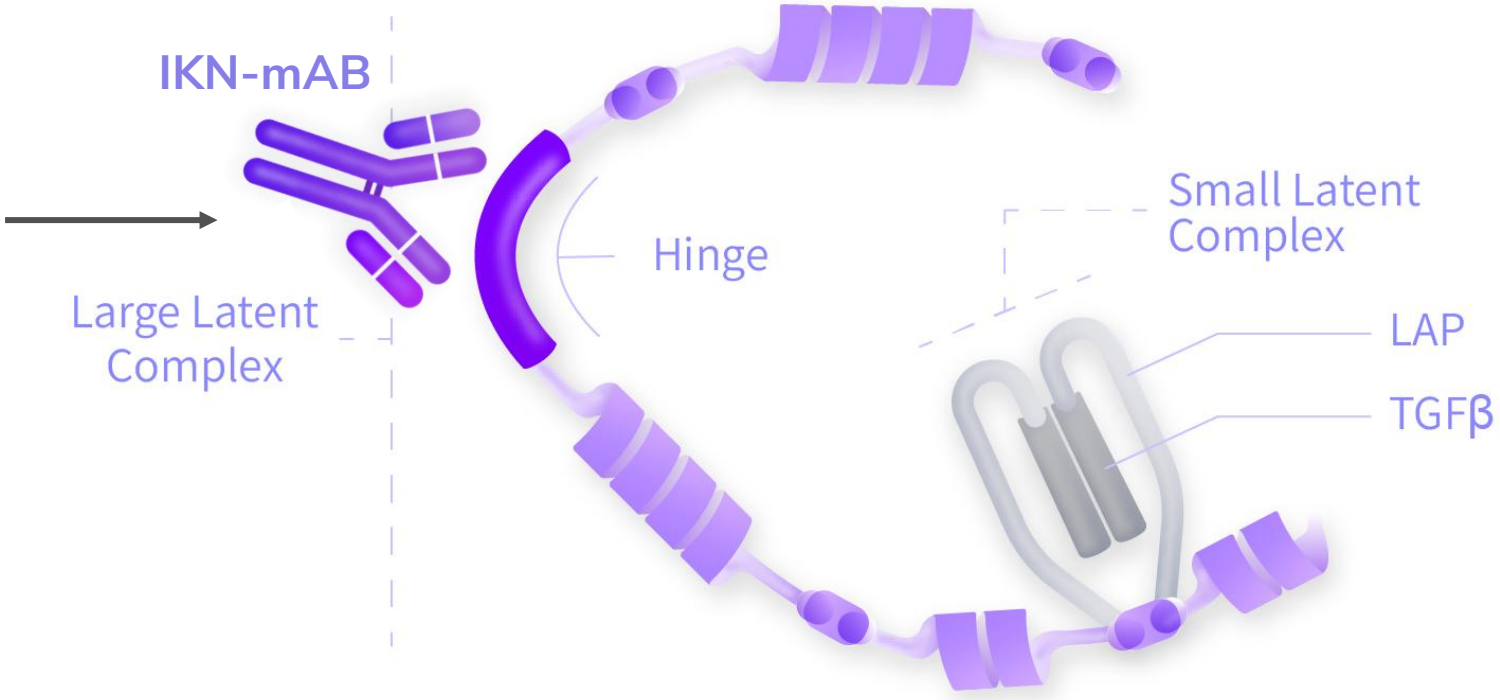
Genome-wide mapping platform led to discovery of LTBP4 as a modifier muscle disease severity

Anti-LTBP4-TGF-β complex **Mechanism of Action (MOA)**



IKN-mAb protects LTBP4's hinge region, stabilizing the large latent complex and reducing active TGF-β

Latent TGF-β binding protein 4 (LTBP4) complex



Transforming Growth Factor Beta (TGF-β) is a known master regulator of fibrosis

Role in tissue:

LTBP4 / TGF-β complex impacts cell growth, differentiation, and ECM composition in **many tissues** including those most affected in **DMD**

Muscles:

Plays a crucial role in maintaining muscle structure, function, and repair by regulating TGF-β signaling

Cardiovascular System:

Expressed in the heart and vessels contributing to cardiac function and integrity

Lung:

Highly expressed in lung tissue where it plays a role in lung development, elasticity, and fibrosis

Protective LTBP4 genomic signals in humans and mice, further **validate target**

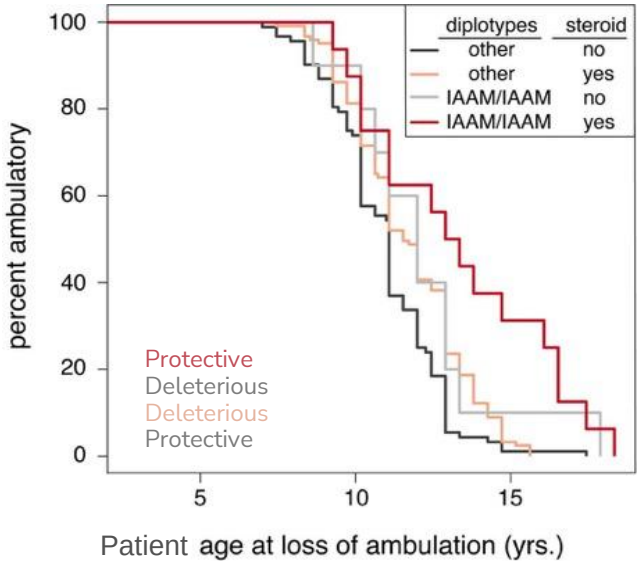
LTBP4 genetically modifies muscular dystrophy progression in mice

LTBP4 genetically modifies the severity of DMD in humans

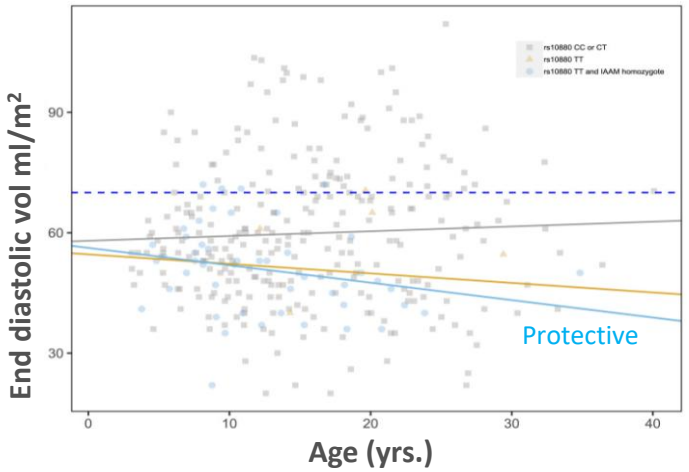
LTBP4 genotype predicts ambulation outcomes in DMD

LTBP4 genotype predicts cardiac function outcomes in DMD

LTBP4 genotype predicts DMD ambulation



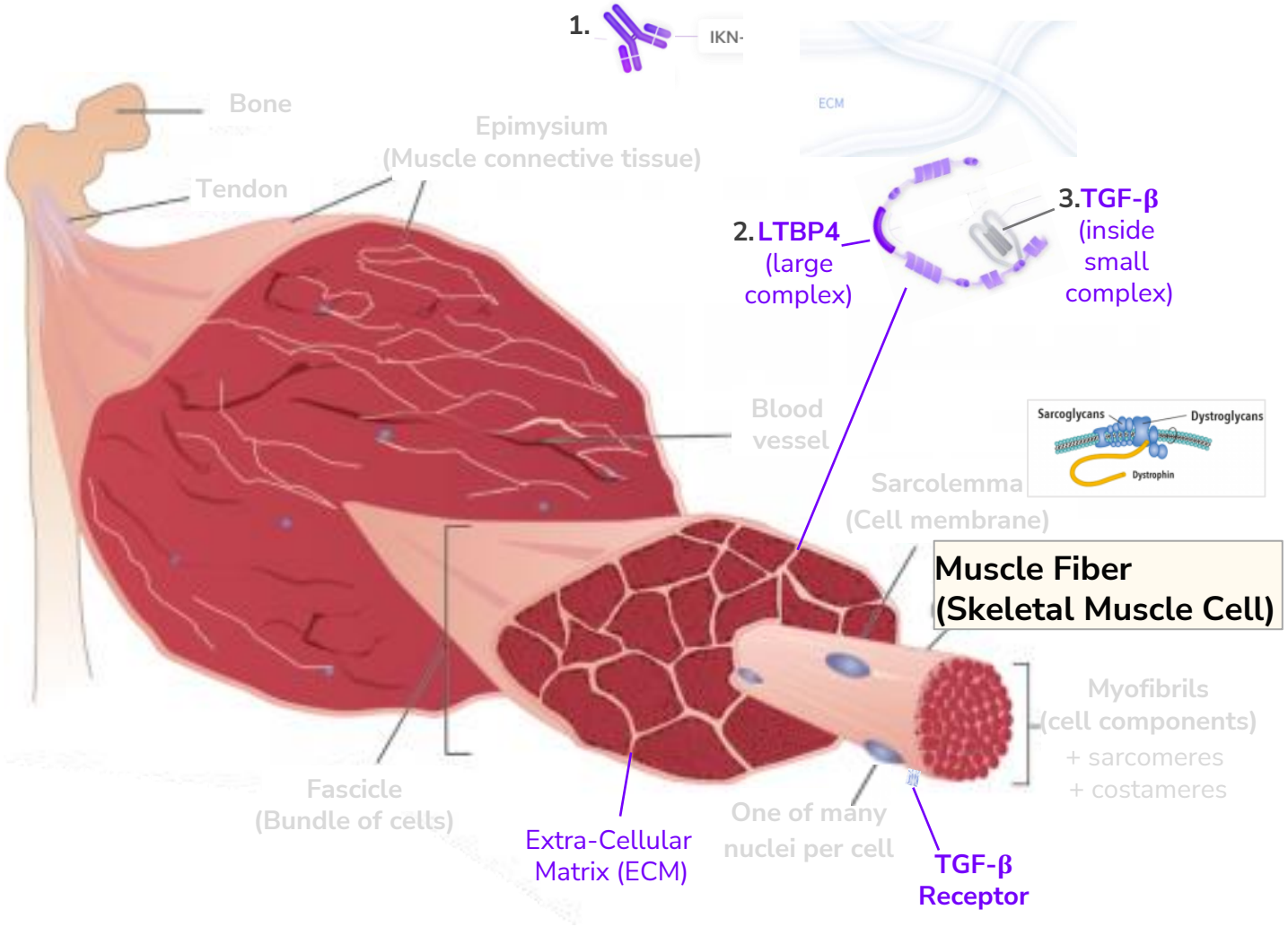
LTBP4 genotype predicts cardiac outcomes



Protective LTBP4 prolongs ambulation and improves cardiac function in humans with DMD

Our lab: Demonbreun et al. Sci Transl Med. 2021 ; Ceco, E. et al. Sci Trans Med 2014 ; Flanigan K, et al. Ann Neurol. 2013 ; Lamar, KM et al. Plos Genet 2016 ; Ceco, E. et al. Sci Trans Med 2014
Other labs: Heydemann et al JCI 2009 ; Lamar et al. PLoS Genet 2016 ; van den Bergen, JC et al. J Neurol Neuro Surg 2015 ; Bello, L. et al. Ann Neurol 5015; Bello, L. et al. J Neuromuscul Dis 2024

Understanding **extracellular** LTBP4 localization for **on-target** IKN-mAb binding

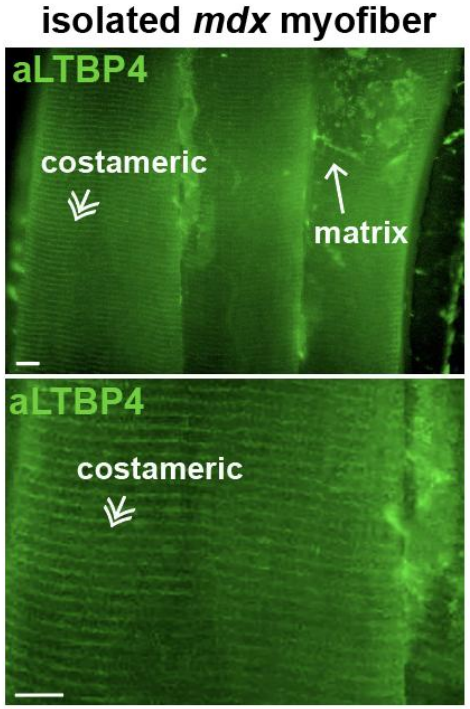


1. mAbs administered **systemically** (IV or SC)

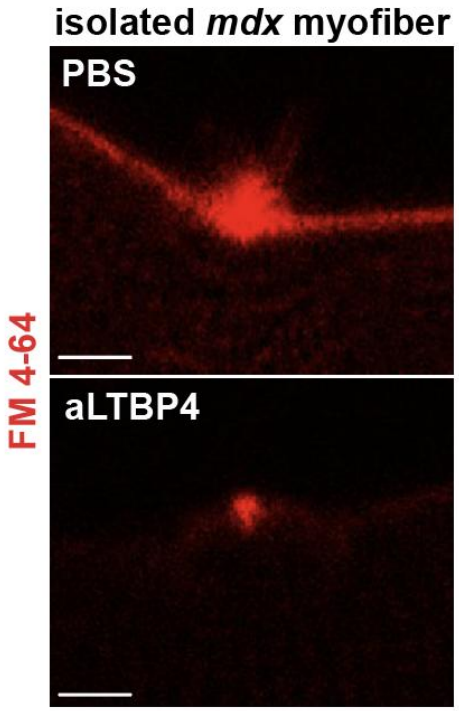
2. IKN mAb's target LTBP4 residing within the skeletal muscle

3. **LTBP4** complex keeps **TGF-β** inactive and anchored in the Extracellular Matrix (ECM) of muscle preventing fibrosis accumulation

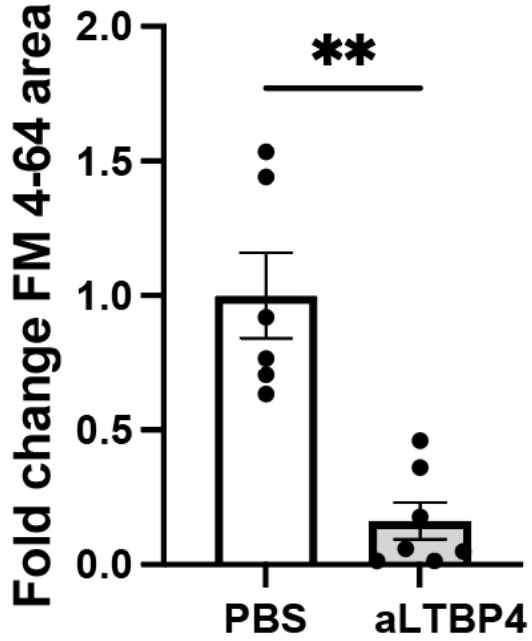
Anti-LTBP4 IKN-mAB binds LTBP4 and **protects** muscle membrane **from injury**



IKN antibody binds to LTBP4 on muscle fibers in a specific manner



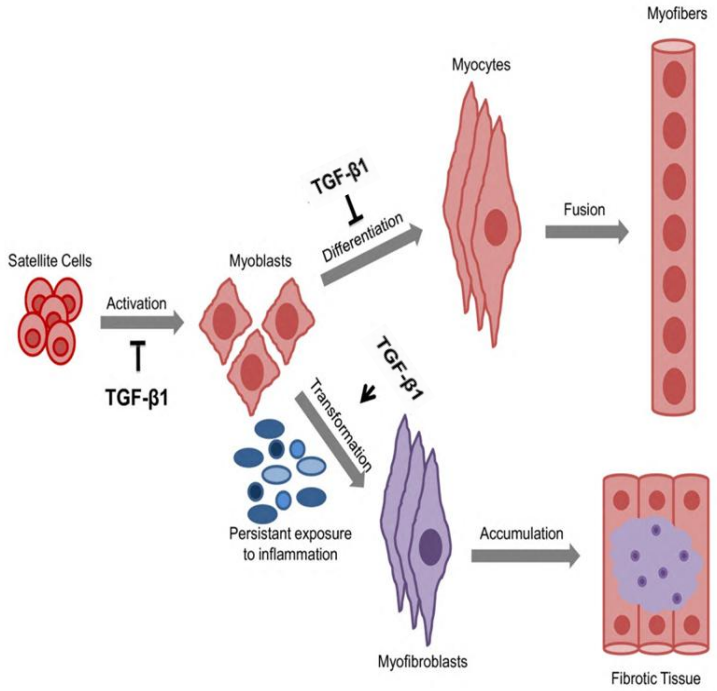
IKN improves muscle membrane resealing after laser injury



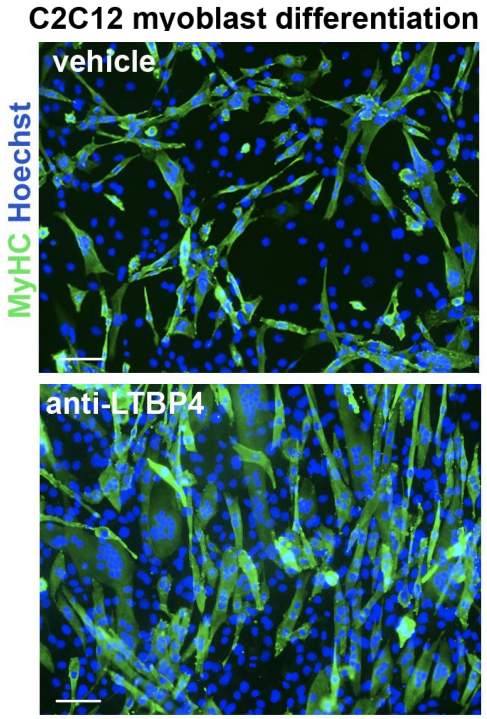
80% reduction in muscle membrane injury with IKN following laser injury

Anti-LTBP4 binds to the muscle membrane and enhances muscle membrane stability

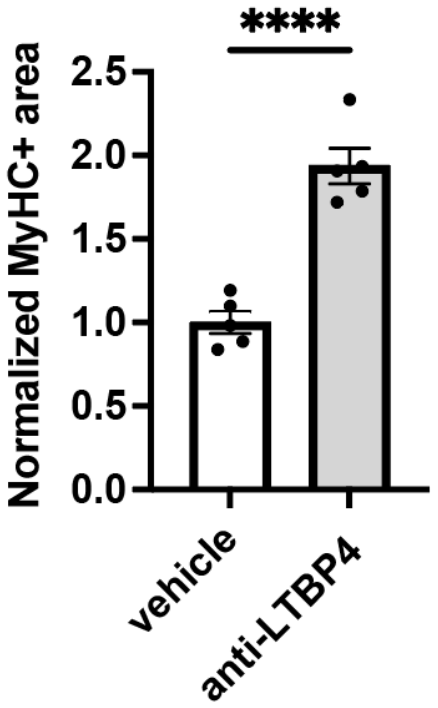
In-vitro studies confirm that anti-LTBP4 IKN-mAB **enhances muscle growth**



Excess TGF-β promotes fibrosis formation and inhibits muscle differentiation



IKN antibody leads to increased myoblast fusion and differentiation



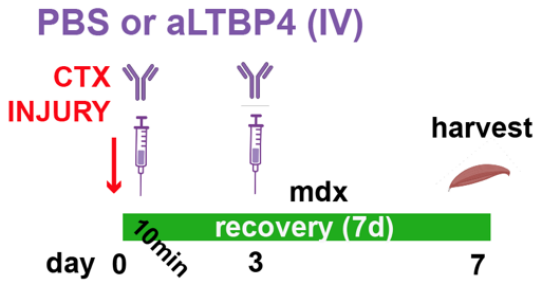
2-fold increase in differentiation with IKN mAbs present

Anti-LTBP4 administration sequesters TGF-β promoting muscle fusion and differentiation

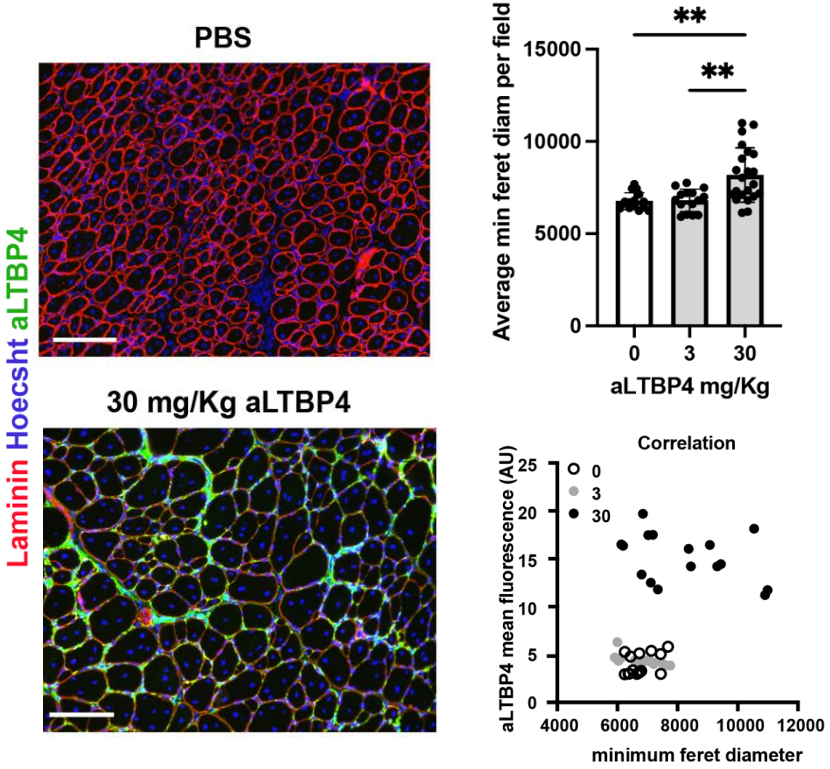
Confidential & proprietary data; Unpublished data; Left graph adapted from Burks Skel Muscle 2011

In-vivo efficacy and MOA:

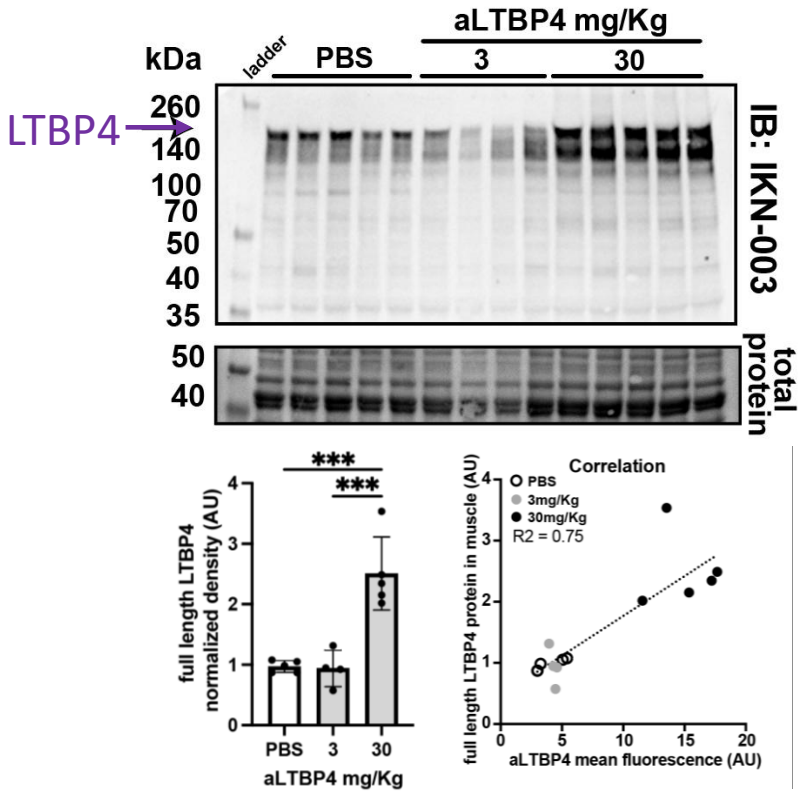
Anti-LTBP4 IKN-mAb **enhances muscle recovery** in a dose-dependent manner



Recovery from cardiotoxin injury relies on both membrane resealing and muscle regeneration



IKN muscle deposition correlates with larger muscle fibers after injury

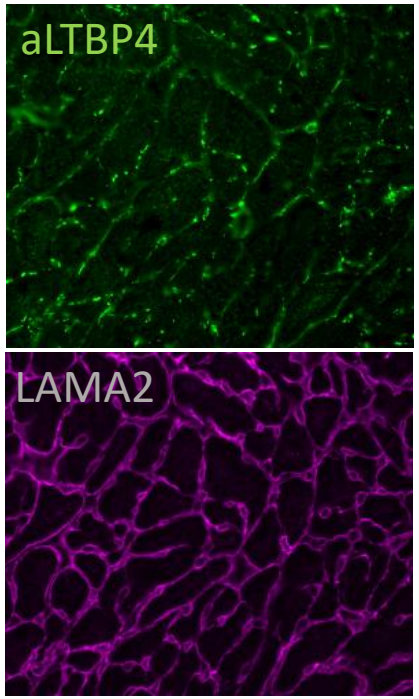


IKN stabilizes LTBP4 in muscle *in vivo*

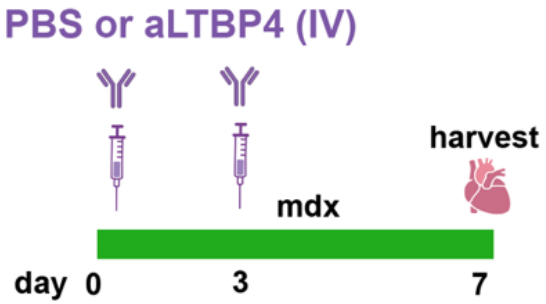
anti-LTBP4 administration stabilizes full-length LTBP4 and promotes repair of dystrophic muscle after cardiotoxin injury

In-vivo MOA:

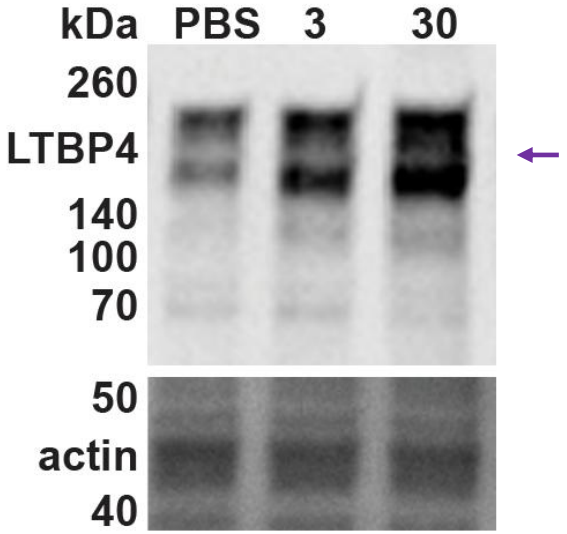
Anti-LTBP4 IKN-mAb binds to and stabilizes full-length LTBP4 **in the heart**



On-target binding of anti-LTBP4 in heart



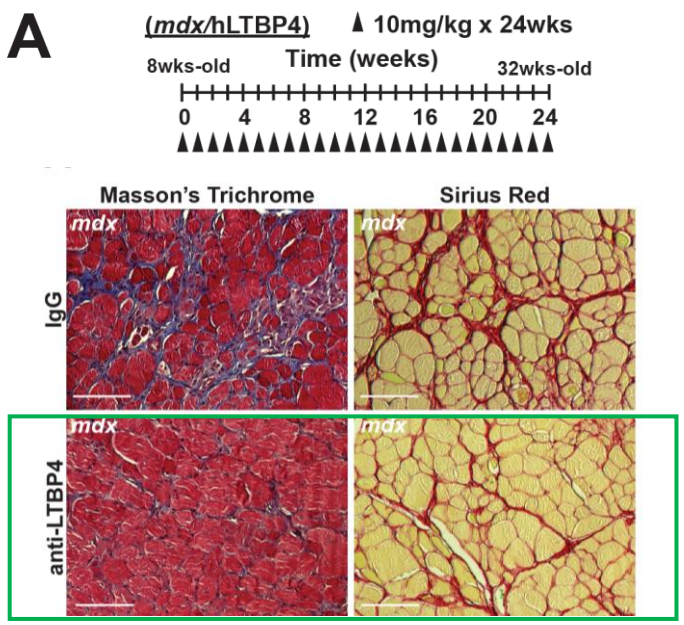
Administration of anti-LTBP4 to assess MOA in the heart



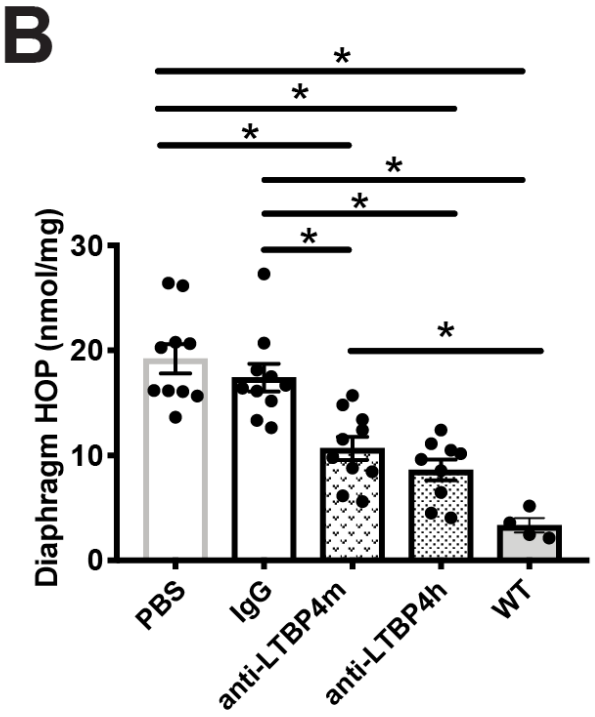
IKN stabilizes full-length LTBP4 in heart *in vivo*

Anti-LTBP4 antibody localizes to the heart and protects LTBP4 hinge from cleavage

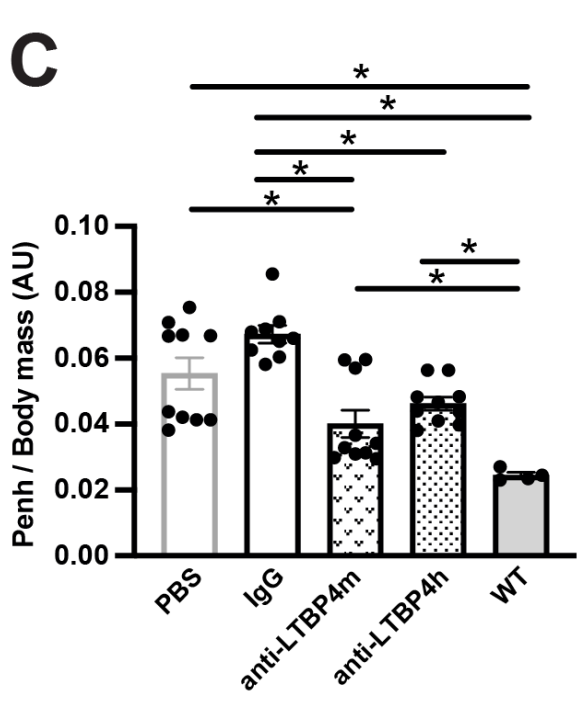
In-vivo efficacy shown in DMD mouse model, shows improvement in breathing



Diaphragm muscles had reduced fibrosis with a 6 months of anti-LTBP4 treatment



Statistically significant improvement in diaphragm muscle fibrosis after treatment



Reduced fibrosis was associated with improved breathing function

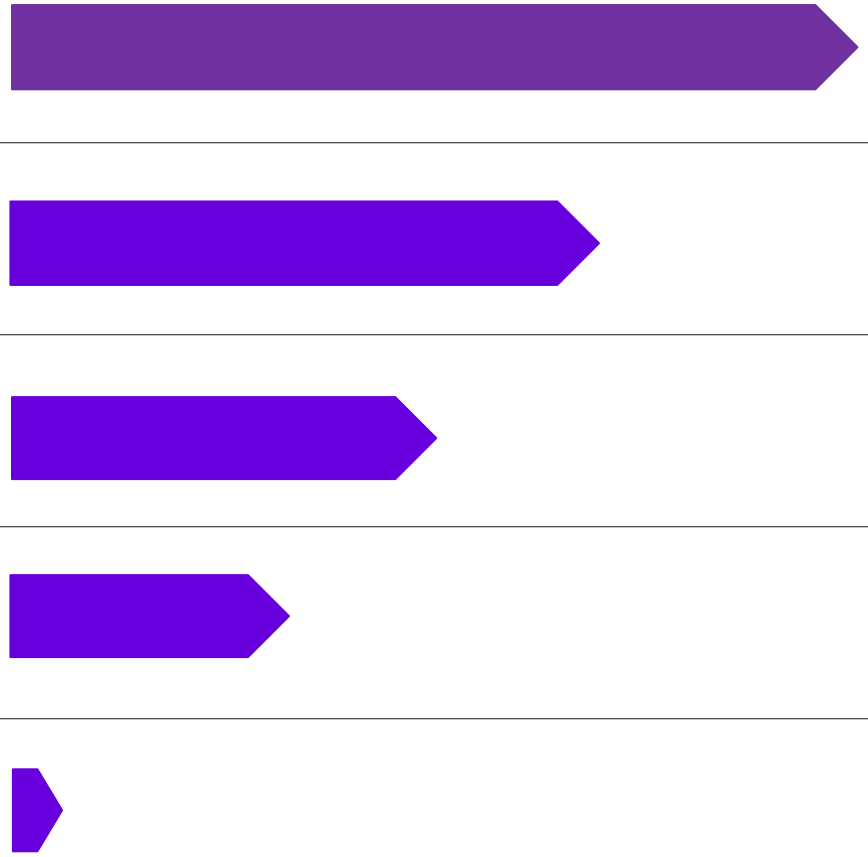
Long-term anti-LTBP4 administration reduced muscle fibrosis and enhanced muscle function

Demonbreun et al. Sci Transl Med. 2021;

Mono- & combination therapies irrespective of disease cause mutation

LTBP4 Pipeline of antibody therapeutics for different indications

Indication	Discovery	Preclinical	IND	Clinical
Duchenne Muscular Dystrophy (DMD)				
Limb Girdle Muscular Dystrophy (LGMD | BMD)				
Muscle Growth and Regeneration (Sarcopenia)				
Idiopathic Pulmonary Fibrosis (IPF)				
Fibrotic Diseases (e.g., heart fibrosis, cancer TME)				



Fundraising for $15M Series A for DMD program, with a planned follow-on estimate of $30M Series B

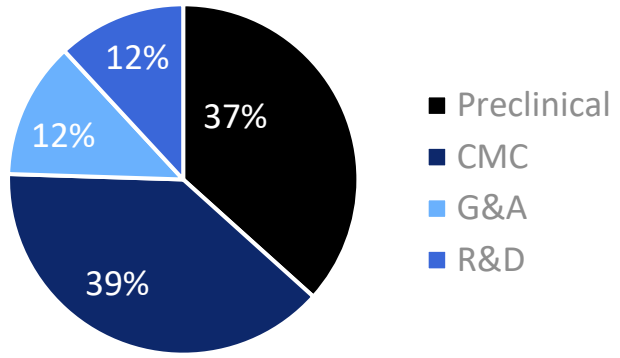
Investment objective for $15M Series A to take us through to First in Human (FIH)

- Raised **$1.6M** to date through a pre-seed and seed note

- **Non-dilutive capital:**
  $3M NIH Blueprint award via UG3 mechanism, to support antibody candidate selection & optimization;
  Award of **multi-million award** through the NIH-UH3 mechanism for IND-enabling studies through FIH

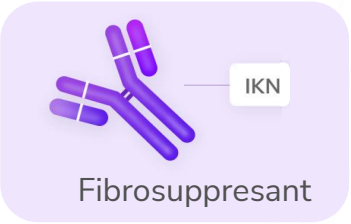
- Seeking **$15M** in Equity as part of a Series A round
  - First tranche of funding will be utilized for CMC process development and pre-IND package support
  - Second tranche of funding for GMP manufacturing and FIH

	Series A
Amounts (USD)	$15M (tranched)
Timing	8 months
Milestones	CMC processes GMP Mfg, GLP Toxicology IND filing, FIH readiness



Use of Funds (Series A)

Executive summary for Ikaika Therapeutics



First in class anti fibrotic biologics

- ✓ Robust **IP portfolio with** issued patents
- ✓ Significant non-dilutive funding for translational activities **for development of mAb therapy for DMD**
- ✓ Partnership with **Northwestern and Adimab**
- ✓ Led by **experts** Drs. McNally and Demonbreun
- ✓ Seeking **$15M in equity** as part of a Series A round
  - Funding will be utilized for CMC process development, GMP manufacturing and GLP assays IND-enabling studies

Robust target validation and preclinical data

- ✓ Genetic signals highlighted hinge region of **novel target validated** as a therapeutic target in genome-wide mapping
- ✓ **Fast-paced preclinical phase,** for antibodies against a novel target latent TGF-β binding protein 4 (LTBP4)
- ✓ Anti-LTBP4 biologics have **differentiated MOA** that improves musculoskeletal, cardiac and pulmonary function and reduces fibrosis in DMD animal models
- ✓ Developed as **monotherapy or combination therapy;** subtype agnostic and applicable for all Muscular Dystrophies

IKAIKA Northwestern Medicine

IKAIKA
Therapeutics

Advancing therapies designed from genetic signals

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Science Contact:
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Appendix

Ikaika Executive Leadership Team: Extensive Expertise In Muscular Dystrophy

Elizabeth McNally, MD, PhD
CEO

- Human geneticist, Cardiologist, KOL
- Director, Center for Genetic Medicine
- Professor, Medicine/Cardiology, Biochemistry & Molecular Genetics, Northwestern Medicine

Alexis Demonbreun, PhD
CSO

- Muscular Dystrophy Researcher, Associate Professor of Pharmacology,
- Center for Genetic Medicine, Northwestern University

Dimitra Georganopoulou, PhD
CBO

- Early-stage Commercialization Expert
- Translational projects operations
- Early-stage fundraising experience
- Qral Ventures, General Partner

Ikaika's advisors and infrastructure

BUSINESS ADVISORS

Chih Kao Hu | Board Member
- Biotech leader with extensive **commercialization** in rare diseases
- CEO of BluedotBio and Window Therapeutics and innovator of Angiomax and contributions to rTPA development (Retavase)
- Managing partner of Qral Ventures, investment arm of Qral Group

Pam Garzone | Industry advisor
- Chief Development officer at Anixa Biosciences
- Pharmaceutical Industry Leadership & Expert in Clinical Research
- Previously with Elan, Genentech and Pfizer Therapeutics

Michael Day | Regulatory
- Senior Director, **Regulatory Affairs**, PharmaLex
- Global product development for biologics
- Multiple regulatory submissions, inc. INDs and BLAs

Eric Schiffhauer | Venture advisor
- Entrepreneurial Executive In Residence, CBC Biotech commercialization leader, drug discovery ventures expert
- Previously with NU's INVO and Deerfield Management

NETWORK THROUGH BLUEPRINT

Adimab

mAb Development
- Antibody drug discovery and target validation
- **Target validation and In-vitro efficacy**
- Antibody sequence optimization

Just EVOTEC BIOLOGI

GMP | CMC- Manufacturing
- Expert biomanufacturing innovation, formulation research
- **Continuous mAb manufacturing**
- CMC, bioproduction innovation & strategic partnerships

VCLS Voisin Consulting Life Sciences

Regulatory / Quality
- Regulatory consultation for US and ex-US submission
- **Pre-IND package and preclinical strategy**
- CMC Toxicology and clinical research planning consultation

inotiv analyze. answer. advance.

CRO
- Non-clinical development services
- **In-vivo safety assessment and analytical support**
- IND enabling studies development and support

Active Patent Portfolio

Ctry	Title	Patent No.	App. No.	Filed	Status	Expiration
US	**Anti-Latent Transforming Growth Factor Binding Protein (LTBP4) antibodies and uses thereof**		**63/764,259**	**2/27/2025**	**Pending**	**--**
US	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)		17/219,845	**3/31/2021**	Pending	--
US	Mitigating tissue damage and fibrosis via latent transforming growth factor beta binding protein (LTBP4)	**US 9,873,739-B2**	13/957,100	**1/23/2018**	**Granted**	**8/1/2033**
US	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)		61/678,564	8/1/2012	Expired	--
WO	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	2880053	13/835,243.0	8/1/2013	Issued	8/1/2033
AU	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	2013313282	2013/313,282	8/1/2013	Issued	8/1/2033
AU	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)		2021/200783	8/1/2013	Pending	--
CA	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)		CA 2 880 649	8/1/2013	Allowed	--
DE	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	602013066304.1	13/835,243.0	8/1/2013	Issued	8/1/2033
EP	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	--	2015-2849.4	8/1/2013	Published	--
HK	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	--	--	--	Pending	--
HK	Mitigating Tissue Damage And Fibrosis Via Anti-LTBP4 Antibody	1211307	15/112,163.9	8/1/2013	Issued	8/1/2033
IN	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	--	898/DELNP/2015	8/1/2013	Pending	--
IT	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	502020000046207	13/835243.0	8/1/2013	Issued	8/1/2033
PC	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	--	PCT/US13/53255	8/1/2013	Expired	--
US	Mitigating Tissue Damage And Fibrosis Via Latent Transforming Growth Factor Beta Binding Protein (LTBP4)	9,873,739	13/957,100	8/1/2013	Issued	8/1/2033