KTIN Therapeutics – One-Pager

Transforming Human Health with Osteocalcin Peptide Analogs
$2M Seed Round | Columbia University Spinout

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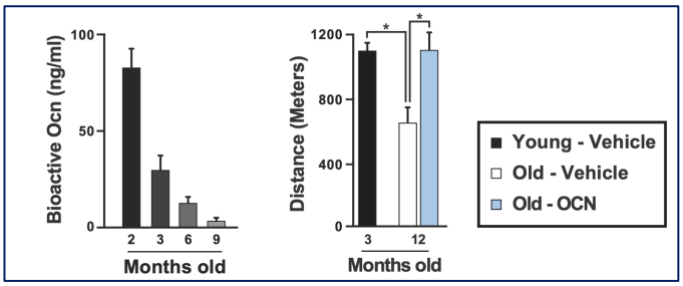
The Problem

- **Muscle decline**:
  - *Sports recovery* – athletes & rehab patients need faster repair.
  - *Sarcopenia* – affects >200M aging adults worldwide.
  - *Cachexia* – severe muscle wasting in cancer & chronic illness.

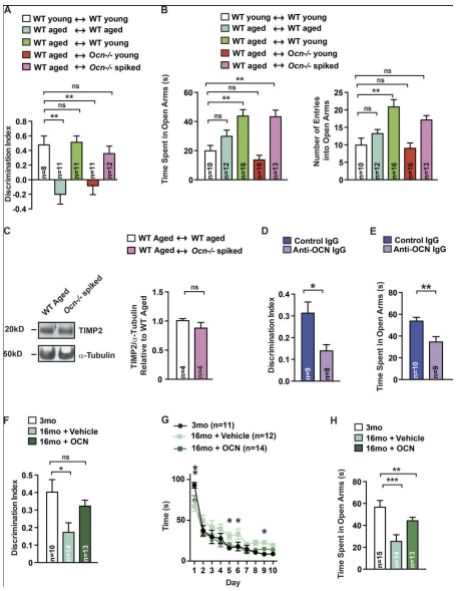


OCN corrects the age-related decline in exercise – Karsenty, Cell Metab 2016

- **Cognitive decline**: Growing burden of MCI and Alzheimer's, Parkinson's Cognitive Decline.
- **Metabolic diseases**: T2D, obesity, NAFLD costing trillions globally.
- **Rare neuromuscular diseases**: LGMD, SMA, OI and related disorders with no cures.

Our Solution

- **Osteocalcin Peptide Analogs (OCN-PAs):** Novel, patent-protected engineered peptides mimicking a **bone-derived hormone**.
- **Validated by 20+ years of science, $10M+ NIH funding, and 150+ publications (Karsenty, Columbia).**
- **Multi-modal benefits:**
  - Stimulates **muscle regeneration & endurance**.
  - Improves **cognitive performance** via neurotransmitter modulation.
  - Enhances **glucose metabolism & insulin sensitivity**.
- **Proven modality:** Peptide analogs (GLP-1, insulin, PTH) have delivered blockbuster drugs.
- **Natural, safe, scalable** with strong IP protection.



OCN is sufficient to improve cognitive function and anxiety-like behaviors – Karsenty, JEM 2017

Market Opportunity

- Sports recovery & performance: **$10B+**
- Sarcopenia / frailty: **$20B+**
- Cachexia: **$5B+**
- Cognitive decline: **$20B+**
- Metabolic diseases: **$50B+**
- Rare neuromuscular: Orphan designation, premium pricing

Total Addressable Market: $100B+

Pipeline Snapshot

Program	Indication	Stage → Next Milestone
KTIN-100	Muscle (sports recovery, sarcopenia, cachexia)	Discovery → Preclinical
KTIN-200	Cognitive decline (MCI, Alzheimer's support)	Discovery → Preclinical
KTIN-300	Metabolic (T2D, obesity, NAFLD)	Discovery → Preclinical
KTIN-R	Rare bone and neuromuscular (LGMD, SMA, TBA)	Exploratory

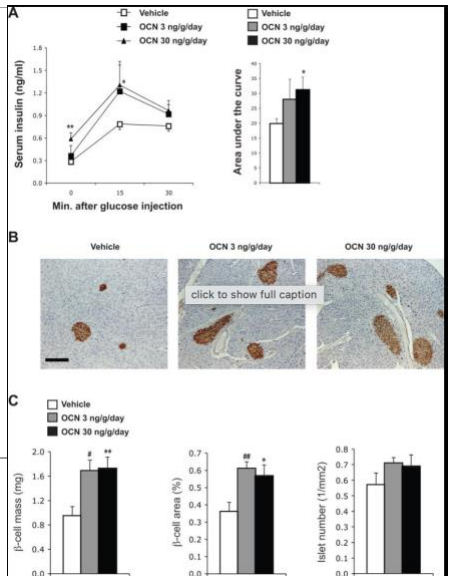
Competitive Advantage

- **First-in-class osteocalcin peptide analogs**.
- **Science-first validation**: Columbia discovery + $10M+ NIH grants.
- **Multi-domain benefit**: Muscle > Cognition > Metabolism > Rare.
- **Strong IP moat**: Patentable engineered peptides.
- **Lower safety risk** vs. synthetic drugs or biologics.

Human studies support Dr. Gerard Karsenty's seminal work on osteocalcin. Refer to the attached references for supporting evidence.

Investment Opportunity

Ask: $2M seed → 18-month preclinical proof-of-concept.
Plan: Synthesis, optimization, preclinical studies → IND-ready candidate.
Exit: Acquisition/licensing by leaders (Novo Nordisk, Lilly, Pfizer, Amgen).
ROI: 10x+ through partnerships, licensing, and rare disease opportunities.



Daily injections of osteocalcin increase insulin secretion and β-cell mass in wild-type mice – Karsenty, Bone 2013

Recent studies in Humans validating Osteocalcin Role

- Levinger I, Scott D, Nicholson GC, Stuart AL, Duque G, McCorquodale T, Herrmann M, Ebeling PR, Sanders KM. Undercarboxylated osteocalcin, muscle strength and indices of bone health in older women. Bone. 2014 Jul;64:8-12.
- **Summary:** This study found that **undercarboxylated osteocalcin** is positively associated with both muscle strength and bone mineral density in older women, suggesting it may play a role in the bone-muscle relationship.

- Liu, Shuying, et al. "Association of serum osteocalcin with bone microarchitecture and muscle mass in Beijing community-dwelling postmenopausal women." Endocrine 84.1 (2024): 236-244.
- **Summary:** This research indicates that serum **osteocalcin** levels are positively correlated with bone microarchitecture and muscle mass in postmenopausal women, suggesting a potential role for osteocalcin in maintaining both skeletal and muscular health.

- Chen, Xi, et al. "Vitamin D status and its associations with bone mineral density, bone turnover markers, and parathyroid hormone in Chinese postmenopausal women with osteopenia and osteoporosis." Frontiers in Nutrition 10 (2024): 1307896.
- **Summary:** This study, while focusing on vitamin D, identifies **osteocalcin** as a key bone turnover marker and explores its relationship with bone mineral density and parathyroid hormone in Chinese postmenopausal women with low bone mass.

- Vitale, Jacopo Antonino, et al. "Circulating carboxylated osteocalcin correlates with skeletal muscle mass and risk of fall in postmenopausal osteoporotic women." Frontiers in Endocrinology 12 (2021): 669704.
- **Summary:** This paper demonstrates that circulating levels of **carboxylated osteocalcin** are positively correlated with skeletal muscle mass and negatively correlated with the risk of falls in postmenopausal women with osteoporosis.

- Zheng WB, Hu J, Zhao DC, Zhou BN, Wang O, Jiang Y, Xia WB, Xing XP, Li M. The role of osteocalcin in regulation of glycolipid metabolism and muscle function in children with osteogenesis imperfecta. Front Endocrinol (Lausanne). 2022 Aug 2;13:898645.
- **Summary:** This article explores how **osteocalcin** plays a significant regulatory role in glycolipid metabolism and muscle function, specifically in children afflicted with osteogenesis imperfecta.

- Liu, D-M., X-Z. Guo, H-J. Tong, B. Tao, L-H. Sun, H-Y. Zhao, G. Ning, and J-M. Liu. "Association between osteocalcin and glucose metabolism: a meta-analysis." Osteoporosis International 26, no. 12 (2015): 2823-2833.
- **Summary:** This meta-analysis synthesized data from multiple studies and found a significant positive association between circulating **osteocalcin** levels and improved glucose metabolism, supporting its role as a bone-derived hormone that influences blood sugar regulation.

- Zeng, Hailuan, Jieyu Ge, Wenjie Xu, Hui Ma, Lingyan Chen, Mingfeng Xia, Baishen Pan, Huandong Lin, Sijia Wang, and Xin Gao. "Type 2 diabetes is causally associated with reduced serum osteocalcin: a genomewide association and mendelian randomization study." Journal of Bone and Mineral Research 36, no. 9 (2020): 1694-1707.
- **Summary:** This genetic study provides evidence for a causal link, showing that **type 2 diabetes** is associated with lower serum osteocalcin, which supports osteocalcin's role in glucose regulation.

- Lin, Xuzhu, Tara C. Brennan-Speranza, Itamar Levinger, and Bu B. Yeap. "Undercarboxylated osteocalcin: experimental and human evidence for a role in glucose homeostasis and muscle regulation of insulin sensitivity." Nutrients 10, no. 7 (2018): 847.
- **Summary:** This review highlights both experimental and human evidence supporting the role of **undercarboxylated osteocalcin** in maintaining glucose homeostasis and regulating insulin sensitivity within skeletal muscle.

Rare Bone Diseases with Muscle Weakness: Adjunct Therapy Opportunity

The Osteocalcin Advantage in Rare Diseases

Triple-Mechanism Therapeutic Action:

- **Myocyte Function Enhancement:** Direct stimulation of muscle fiber contractility and endurance capacity through calcium signaling modulation
- **Neuroprotective Effects:** Neurotransmitter regulation (GABA/glutamate balance) supporting cognitive function and potentially addressing neurological complications
- **Metabolic Homeostasis:** Glucose-insulin axis optimization through enhanced β-cell function and peripheral insulin sensitivity

Clinical Rationale:

- Zheng et al. (2022) demonstrated OCN's regulatory role in glycolipid metabolism and muscle function in pediatric osteogenesis imperfecta
- Natural bone-derived hormone minimizes off-target effects compared to synthetic therapeutics
- Addresses systemic complications beyond primary disease pathology

Regulatory & Market Advantages:

- Orphan Drug Designation eligibility across multiple rare conditions
- Premium pricing potential ($150K-$750K annually) with strong reimbursement
- Limited competition in bone-muscle interface therapeutics

Target Conditions for KTIN-R Program

Condition	Key Symptoms	Unmet Need	Patients Affected	How OCN Can Address
Osteogenesis Imperfecta (OI)	Brittle bones, muscle weakness, short stature	Current treatments only target bone strength, ignore muscle weakness	~20,000-50,000 (US)	Improve muscle function + bone mineralization + metabolic support
Limb-Girdle Muscular Dystrophy (LGMD)	Progressive hip/shoulder weakness, bone fragility	No disease-modifying treatments available	~1 in 14,500-123,000	Enhanced myocyte contractility + bone preservation + cognitive support
Spinal Muscular Atrophy (SMA)	Severe muscle weakness, bone fractures, respiratory issues	Gene therapies don't address bone complications	~1 in 8,000-10,000 births	Complement gene therapy: muscle function + bone protection + metabolic optimization
Duchenne Muscular Dystrophy (DMD)	Progressive muscle loss, steroid-induced bone loss	Steroids cause severe bone side effects	~1 in 3,500 males	Counter steroid effects: optimize muscle function + bone health + glucose homeostasis
Hypophosphatemic Rickets	Soft bones, muscle weakness, dental issues	Limited efficacy of phosphate/vitamin D supplements	~1 in 20,000 globally	Direct bone mineralization + myocyte enhancement + metabolic regulation

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KTIN-R leverages osteocalcin's unique systemic hormone properties to address the bone-muscle-metabolic axis in rare diseases where current therapies have significant gaps.