

# Mammoth Biosciences

## Category:

Best Startup

## Company Name:

Mammoth Biosciences

## Turnover and/or Funding:

Since its founding, Mammoth Biosciences has raised ~\$465 million, including ~\$365 million in equity capital and \$100 million-plus in non-dilutive funding from leading pharmaceutical and biotechnology partners such as Regeneron, Bayer and Vertex.

## Sub-Category:

Biotechnology

## Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

Founded in 2017 by CRISPR pioneer and Nobel laureate Jennifer Doudna, Trevor Martin, Janice Chen and Lucas Harrington, Mammoth Biosciences is a leader in the rapidly evolving field of genetic medicines. The company's ultracompact CRISPR platform enables gene editing to go beyond ex vivo therapies and limited in vivo applications - propelling the field forward to address areas of greatest unmet need, such as muscle and central nervous system diseases, thereby dramatically increasing the number of patients who could potentially benefit from gene editing treatments.

Mammoth Biosciences achieved unicorn status in just four years, underscoring investor confidence in its gene editing platform and its strong IP position. Building on this momentum, Mammoth has established an unparalleled portfolio of collaborations with major biopharma companies, including Vertex Pharmaceuticals, Bayer AG and most recently, Regeneron Pharmaceuticals

Mammoth is building out its wholly owned pipeline and drug development capabilities in a focused and highly capital-efficient manner to accomplish its long-term vision of bringing permanent genetic cures to transform patients' lives. The company has recently strengthened its leadership team with genetic medicine stalwarts in

translational research, clinical development, manufacturing and regulatory affairs.

Mammoth serves as a model for next-generation platform companies by demonstrating how bold scientific vision - filtered through a pragmatic lens and supported by strategic partnerships and focused execution - can deliver transformative outcomes and build the next great lasting biotech company. The company's pioneering work has earned widespread recognition, including the Endpoints 11 award, Fast Company's Next Big Thing in Tech award, California Life Sciences Pantheon award, among others.

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Familial chylomicronemia syndrome (FCS) is a rare genetic disorder, affecting between 300 - 3000 individuals in the US. It is caused by mutations in genes that regulate triglyceride metabolism, resulting in extremely elevated triglyceride levels. FCS patients experience severe, recurrent acute pancreatitis (AP), leading to frequent hospitalizations and a high risk of cardiovascular disease and other complications. There are currently no treatments for FCS in many countries, and patients are put on a lifelong, ultralow fat diet.

Severe hypertriglyceridemia (SHTG), defined by persistently high triglyceride levels, is more common than FCS, affecting more than 3 million individuals in the US. SHTG increases the risk of AP and cardiovascular disease. Management of SHTG includes dietary fat restriction, weight loss and glycemic control, in conjunction with fibrates, high-dose omega-3s and statins.

Studies have shown that FCS and SHTG lead to increased healthcare expenditure. For example, FCS patients experience approximately 10 episodes of AP during their lifetime, resulting in 80.7 inpatient days and a lifetime cost of \$154,126, on average, per patient. A simulation model found that an intervention which reduces triglyceride levels by 50% in patients, would result in 7.72 fewer episodes of AP, saving an average of \$118,594 in medical costs.

FCS/SHTG patients lack effective, durable treatment options that address the root cause of disease. Mammoth Biosciences' ultracompact CRISPR therapy, MB-111, offers a much-needed therapeutic paradigm shift that moves beyond management to potentially curative interventions that may benefit millions of patients.

## **History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):**

The Nobel Prize-winning discovery of CRISPR gene-editing marked a turning point in medicine. Yet, more than a decade later, its full therapeutic potential remains unrealized by one critical challenge: in vivo delivery to target tissues, especially beyond

the liver. First-generation CRISPR systems, such as Cas9 and Cas12a, are too large to be efficiently packaged into existing viral and non-viral delivery mechanisms, limiting gene-editing to a few diseases that can be targeted via the liver or by ex vivo approaches.

Mammoth Biosciences recognized this limitation and pioneered a new class of ultracompact CRISPR systems, challenging the prevailing belief that smaller systems must compromise on performance. Using advanced metagenomics, high-throughput functional screens and protein engineering, Mammoth developed novel, ultracompact CRISPR systems with superior therapeutic potential, including CasPhi and NanoCas. Their compact size enables delivery in a single AAV vector, leaving room for additional payloads - such as regulatory elements, guide RNAs and partner proteins - required for reverse transcriptase editing, base editing and epigenetic editing. Mammoth is developing all these modalities as alternatives to double-stranded breaks.

By overcoming this delivery challenge, Mammoth Biosciences is unlocking the ability to target a broader range of tissues and diseases. And this isn't just theoretical: Earlier this year, the company unveiled its first ultracompact extrahepatic gene editor, NanoCas, which is just 448 amino acids - approximately one-third the size of first-generation, Cas9-based CRISPR systems.

Mammoth announced new preclinical data showing that NanoCas, delivered via a single AAV vector, efficiently edited the dystrophin gene in mice (up to 40% in quadricep, calf, heart muscle) and in monkeys (up to 30% in skeletal muscle versus < 3% with SaCas9). These editing levels are particularly encouraging given that restoration of approximately 10% of normal dystrophin levels is thought to be sufficient for therapeutic benefit. In vivo editing by NanoCas was well tolerated and minimal off-target editing was reported.

These data are the first demonstration of robust in vivo editing in muscle, a historically hard-to-reach tissue. It also marks a critical step toward realizing CRISPR's full potential to treat a wider spectrum of genetic diseases, such as muscular dystrophies, a group of inherited diseases that cause progressive weakness in the muscles that control movement.

Additionally, Mammoth Biosciences nominated its first clinical development candidate, MB-111 - a potential first-in-class in vivo ultracompact CRISPR therapy aimed at lowering dangerously high triglyceride levels in patients with FCS and SHTG. MB-111 uses CasPhi, delivered to the liver via a lipid nanoparticle, to disrupt the APOC3 gene, a key regulator of lipid metabolism. In mice and monkeys, MB-111 achieves editing efficiencies of ~70% and ~55%, respectively - levels comparable to Cas9 - resulting in a 90% reduction in ApoC3 protein and a 95% drop in serum triglycerides. The therapy was well tolerated and showed minimal editing outside the liver.

With IND-enabling studies planned for 2025, this program marks the first clinical translation of Mammoth's ultracompact CRISPR technology and a major milestone in the evolution of programmable genetic medicines to tackle in vivo genetic disease.

**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

CRISPR is at an inflection point as it moves from experimental breakthroughs to real-world applications, with the first therapies for genetic diseases, such as sickle cell, now reaching patients. While the technology was once heralded as a cure-all for genetic disease, the reality has proven more complex.

First-generation Cas9-based CRISPR systems are too large for efficient delivery via a single AAV vector - the gold standard for targeted in vivo delivery beyond the liver. Consequently, the clinical reach of gene editing has remained confined to only a handful of diseases that can either be treated by ex vivo editing or to those treatable via editing of the liver using lipid nanoparticle-based delivery. This has left other CRISPR companies all focused on the same handful of diseases and unable to deliver on the full promise of the technology. This delivery problem is even more acute for novel gene editing modalities - such as base editing, gene writing, and epigenetic editing - which must deliver not only the CRISPR cargo, but also additional helper proteins for the specific edit type. Unfortunately, this complexity has caused these novel editing modalities to be directed at the same small set of ex vivo and liver targets - areas already crowded with existing approaches.

With Mammoth's ultracompact systems and novel forms of these editing modalities and beyond, the company can - for the first time - deliver any known editing modality in a single AAV, and actually bring these critical technologies to the tissues and diseases that need it the most: diseases such as Alzheimer's, Parkinson's, and Huntington's disease.

Mammoth Biosciences' ultracompact CRISPR systems stand capable of realizing the disruptive potential of these advances by enabling any type of edit to be made in any cell in vivo, thereby significantly expanding the range of diseases that can be treated and dramatically increasing the number of patients who could benefit from genetic medicines. As Mammoth Biosciences' efforts transition from the bench to the clinic, the "mammoth" impact of its ultracompact CRISPR systems could help redefine the future of medicine and deliver on the full promise of CRISPR.

**Please provide appropriate references (PubMed, Abstract, Website):**

RESEARCH PAPERS

1. Harrington et al. Science (2018) DOI: 10.1126/science.aav4294

2. Pausch et al. Science (2020) DOI: 10.1126/science.abb1400

## PRESENTATIONS

3. Chen, J. (2024). \"Developing in vivo Therapeutics with Ultracompact CRISPR Systems\" Keystone Symposium

4. Harrington, L. (2024). \"Reduction in Triglycerides through a Novel Ultracompact CRISPR System: Efficacy in Mouse Models and NHP Studies\" Abstract 15. ASGCT (pp. 8-9)

5. Harrington, L. (2024) \" Ultracompact CRISPR Systems to Overcome the Delivery Problem\" Chardan Annual Genetic Medicines Conference

6. Sper R. (2025) \"Non-Human Primate Muscle Gene Editing Via Single Systemic AAV Delivery of an Ultra-Compact CRISPR Nuclease\" Abstract 205. ASGCT (pp. 199-200)

## PREPRINTS

7. Rauch et al. bioRxiv (2025) DOI: 10.1101/2025.01.29.635576

## PRESS RELEASES

8. Mammoth Biosciences (2025, January 31). \"Mammoth Biosciences Announces New Results on NanoCas - the First Efficient Ultracompact Extrahepatic Gene Editor\" [Press Release]. Businesswire

9. Mammoth Biosciences (2025, May 5). \"Mammoth Biosciences Announces Nomination of MB-111 as First Development Candidate and Appoints Genetic Medicines Veteran Bob D. Brown to Board of Directors\" [Press Release]. Businesswire

## AWARDS

10. Fast Company (2022) \"How Mammoth is chasing CRISPR 2.0 with a smaller pair of scissors\" [Next Big Things in Tech Award]

11. Endpoints News (2022) \"The top private biotechs in pursuit of new drugs. Pushing the envelope with powerful new technologies\" [The Endpoints 11 Award]

12. Biospace (2022) \"Mammoth Biosciences\" [Best Places to Work Award]

13. California Life Sciences (2024) \"Pantheon Awards\" [Pantheon Award]

## MEDIA COVERAGE OF NANOCAS

14. Couzin-Frankel, J. (2025) \"A new 'mini-CRISPR' flexes its editing power in monkey muscles\" Science, 387(6734), 570. DOI: 10.1126/science.adw4916

15. LeMieux, J. (2025) \"AAV Delivered NanoCas CRISPR System Edits Muscle in Non-Human Primates\" Genetic Engineering & Biotechnology. [Article]

16. Jackson, J. (2025) \"NanoCas, a smaller version of CRISPR tested with a single AAV, delivers on-target results\" Phys.org [Article]

## PARTNERSHIPS

17. Mammoth Biosciences (2021, October 26). \"Vertex and Mammoth Biosciences Announce Collaboration to Develop In Vivo Gene-Editing Therapies for Serious Diseases\" [Press Release]

18. Mammoth Biosciences (2024, January 10). \"Bayer and Mammoth Biosciences to Collaborate on Novel Gene Editing Technology\" [Press Release]
19. Mammoth Biosciences (2024, April 25). \"Regeneron and Mammoth Biosciences Collaborate to Pursue Next-Generation CRISPR-Based Gene Editing for Multiple Diseases\" [Press Release]

## PATENTS

Mammoth Biosciences has filed over 50 PCT patent applications that are directed to ultracompact CRISPR therapeutic systems. In addition, Mammoth exclusively licenses select related IP from the University of California. Exemplary IP includes:

### 20. UC licensed patents:

US Pat. No. 12,312,616, US Pat. No. 11,578,313, US Pat. No. 11,685,909, JP7672445, JP7239725, JP7629474, CN201880084919, and AU2018358051

### 21. Mammoth-owned patents:

US Pat. No. 12,077,775 and US Pat. No. 11,814,620

### 22. Mammoth-owned PCT applications:

WO/2023/220570 (engineered nucleases) WO/2025/072763 (ultracompact RT editing); WO/2023/004430 (single AAV systems), WO/2023/205773 (DMD guides); WO/2025/019613 (DMPK guides); WO/2024/182444 (APOC3 guides); WO/2024/173699 (SMN2 guides); WO/2024/263707 (SOD1); WO/2025/024285 (C9ORF72 guides); and WO/2024/137767 (DUX4 guides)

### 23. Mammoth owned patent applications pending in the US, Europe, and beyond.

## WEBSITE AND CORPORATE DECK

24. <https://mammoth.bio/>

25. Mammoth 2025 corporate presentation

## References File Document upload:

**2 Mammoth Biosciences Pausch et al Science 2020.pdf**

**1 Mammoth Biosciences Harrington et al Science 2018.pdf**

**4 Mammoth Biosciences Presentation PowerPoint Mammoth Biosciences Harrington L 2024 Reduction in Triglycerides through a Novel Ultracompact CRISPR System Efficacy in Mouse Models and NHP Studies.pdf**

**3 Mammoth Biosciences Chen J 2024 Developing in vivo Therapeutics with Ultracompact CRISPR Systems Keystone Symposium.pdf**

**4 Mammoth Biosciences Presentation PowerPoint Mammoth Biosciences Harrington L 2024 Reduction in Triglycerides through a Novel Ultracompact CRISPR System Efficacy in Mouse Models and NHP Studies.pdf**

**5 Mammoth Biosciences Harrington L 2024 Ultracompact CRISPR Systems to Overcome the Delivery Problem Chardan Annual**

**Genetic Medicines Conference.pdf**

**6 Mammoth Biosciences Presentation PowerPoint Sper R 2025  
NonHuman Primate Muscle Gene Editing Via Single Systemic AAV  
Delivery of an UltraCompact CRISPR Nuclease.pdf**

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**8 Mammoth Biosciences Mammoth Biosciences 2025 January 31  
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