

→ Mark your confusion.

→ Purposefully annotate the article (1-2 mature, thoughtful responses per page to what the author is saying)

→ Write a 250+ word response to the article.

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## The rise of legal cannabis

By Dan McCarthy for Morning Brew, September 19, 2022

While the Apollo program of the 1960s is typically remembered for being the first time a human landed on an alien surface (or for kickstarting the complicated and ridiculous conspiracy theory that the moon landing never happened), the original moonshot has also had a more direct, albeit lower-profile, impact on our daily lives.

In order to make the Apollo missions happen, a whole bunch of foundational technologies had to be invented or improved upon. Telecoms satellites, GPS, microchips—these technologies may not have developed as rapidly, or at all, if it hadn't been for the rallying cry of the space race. Today, the microchip industry alone is worth half a trillion dollars, and critical enough that a chip shortage is currently stymieing production of everything from cars to washing machines.

Alongside gene-editing pioneer and Harvard professor George Church, serial entrepreneur Ben Lamm is trying to architect his own version of a moonshot with a new company called Colossal, which aims to re-create and rewild the woolly mammoth. Colossal is using the gene-editing technology CRISPR to come up with a proxy of the shaggy-haired megafauna that vanished around 4,000 years ago. The company also intends to commercialize its biotech discoveries under a license agreement with Harvard, which excludes human applications.

“Just like in the Apollo program, where a lot of the technologies that were created were able to be monetized over time,” Lamm told Emerging Tech Brew, Colossal is “very confident that there will be some pretty interesting breakthroughs in the world of genomics, multiplex editing[...], and in software databases for genetic reconciliation.”

The global biotech industry is already worth \$753 billion, according to Grand View Research, and projected to grow to over \$2 trillion by 2028. Even capturing a small slice of an industry that large would help Colossal sustain itself, though Lamm told us the company “has runway for quite some time” with the \$15 million seed round it raised from 12 funders, including billionaire Thomas Tull and venture firm Draper Associates. He expects that Colossal can and will attract more funding when and if needed.

The company also has a dizzying list of ancillary objectives. It wants to inspire public interest in STEM, create technologies that can be used to rewild other species, combat climate change by restoring carbon-capturing biodiversity, prompt discussion in bioethics, and advance the field of conservation. The idea is that if Colossal achieves its mammoth moonshot, the rest of this will happen along the way.

### Why the woolly?

The notion of re-creating and rewilding the woolly mammoth has its roots in the decades-old idea of introducing Asian or African elephants to regions where large creatures used to roam, like North America or Europe, according to Greg Kaebnick, a scholar and editor at bioethics research institute the Hastings Center. But the idea of actually re-creating the mammoth—or a proxy of it—only became tangible in the last decade or so.

Church has been working on woolly mammoth revival at Harvard for nearly a decade, based in part on a 2015 grant of \$100,000 from Peter Thiel. And scientists at Penn State University have discussed the near-term possibility of cloning a mammoth since at least 2010.

“I’m very sympathetic to the idea of trying to recover lost natural phenomena—missing species, the ecosystems that were built around those species,” Kaebnick told Emerging Tech Brew. “I am very skeptical that we’d be able to bring back the actual species—I think the [phrase] ‘bringing back’ is not right. Really, it’s more like creating something brand new that’s similar.”

The mammoth is a good de-extinction candidate for a few reasons, Lamm said. For one, thanks to

permafrost, there are a lot of well-preserved mammoth specimens—that means access to full genome sequences, plus data on how the animals evolved over time. The project can also be viewed as a form of “species extension,” Lamm argued, because, if successful, it would functionally create a form of elephant that can survive in a new habitat.

And in their heyday, mammoths helped stabilize the arctic ecosystem—particularly the all-important permafrost layer. It’s estimated that arctic permafrost contains four times as much carbon as humans have emitted since the Industrial Revolution, and at our current pace of emissions, scientists expect 40% of it to melt by the end of this century. Plus, certain types of plants, like honey-locust trees, evolved specifically to interact with megafauna, Kaebnick said, meaning they would also benefit from the presence of a mammoth-like creature.

### **Don’t say it...don’t say it...A mammoth undertaking**

Lamm said Colossal’s funders are not expecting immediate returns. That’s a good thing. The timeline for the company to even begin rewilding mammoths is 15 years out, Lamm said, assuming all goes well.

“We believe we will be able to have our first calves in four to six years, but then you have to go through socialization, reintroduction, and ensure that you think through all the rewilding aspects of it,” Lamm said. “It is a long-term play—it’s not something that tomorrow we’re going to have mammoths, and the next day there’s going to be 100,000 in the Arctic, and the next day, we’ve revitalized the Arctic and the grasslands.”

But when the opportunity does come up to commercialize a promising technology—like, say, an artificial womb, or multiplex genome engineering tech that can help fight genetic bottleneck in animals with low populations—Colossal has a team of experienced entrepreneurs ready to act. The company is not married to any sort of business model at this point, but will instead treat commercially viable advances on a case-by-case basis, commercializing some within Colossal while maybe also spinning others out.

“We don’t have anything today specifically planned from a monetization perspective, but we do have buckets of ideas,” Lamm said. “We’re focused right now on the really hard science—bringing back the mammoth, and not just bringing it back but successfully rewilding the mammoth, is a large enough initiative that requires our focus right now.”

To get to that end point, Colossal has built a core team of 19 employees, spanning scientific and business roles. It also has access to a growing team of post-doctoral researchers in Church’s Harvard lab, and two advisory boards: One is an “executive advisory board” populated with investors and entrepreneurs, while the other is science-focused, and includes high-profile bioethicists, geneticists, and conservationists.

Colossal’s team, advisors, and funders may not mind the project’s lengthy timeline, but Kaebnick said that it will pose challenges for some of the carbon sequestration and climate-related goals the project lays out for itself. Mammoths did help preserve and even deepen permafrost, Kaebnick said, but in order to make a difference, “You’d need hundreds of thousands really fast.”

He noted that biotech advances like artificial wombs could theoretically accelerate the process, but that it’s not a given. “Even with artificial wombs you’re just not going to create a population big enough to make a significant difference in slowing the melting of permafrost,” Kaebnick said.

For now, Colossal isn’t hung up on those longer-term issues. It’s deep in the world of multiplex editing—a process that uses CRISPR to enact a high volume of genetic edits at once. It’s a balancing act that plays out via a combination of software and lab work, with Colossal-affiliated scientists using CRISPR to edit cells, and then running lab tests to make sure the intended molecular functions show up, all without unintentionally wreaking havoc to some other part of the genome.

Lamm said the team has identified 60+ genes that make the woolly mammoth what it is—tiny ears, cold-tolerant hemoglobin, a shag-carpet-esque coat—and is now figuring out how to provide those traits to a new specimen, based on the elephant genome. The next step, he said, is “getting to the point that we have viable embryos.”

While developing an embryo is a straightforward objective, the path to get there is difficult: In 2017, Church claimed that his Harvard team was just two years away from creating a hybrid elephant-mammoth embryo. Two years after that deadline, he’s still working toward that goal.

And even once it's achieved, there are many more steps to reintroducing a living, breathing mammoth into the wild. Along the way, things can and will go wrong, because frontier science is messy and hard.

Because Colossal intends to let science lead the way, its path to profit—or even revenue—will likely follow a similarly long and unpredictable route. But sticking it out could, like the 1969 Apollo 11 mission, generate benefits that stretch beyond the wonder of witnessing a thing once considered impossible.

“We have to continue to ensure that we're hitting our milestones in the science,” Lamm said. “Separately, I think there's a huge opportunity for us to tell some of these stories. The Apollo program inspired so many people, and we have an opportunity here to bring awareness to climate change, to bring awareness to loss of habitat, to bring awareness to genomics, STEM, and to loss of biodiversity.”

**Response option(s):**

- After reading the article, what is one main idea that you find most remarkable (meaning, "most worthy of a remark" -- so it can be interesting, concerning, confusing, alarming, offensive, etc)? What is it that you find so remarkable? Explain.
- After reading the article, what additional questions do you have? Research these on your own and write about what you find.
- Summarize any point made in the article and respond.