

# A 'fountain of youth' pill? Sure, if you're a mouse

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Renowned Harvard University geneticist David Sinclair recently made a startling assertion: Scientific data shows he has knocked more than two decades off his biological age.

What's the 49-year-old's secret? He says his daily regimen includes ingesting a molecule his own research found improved the health and lengthened the life span of mice. Sinclair now boasts online that he has the lung capacity, cholesterol and blood pressure of a "young adult" and the "heart rate of an athlete."

Despite his enthusiasm, published [scientific research](#) has not yet demonstrated the molecule works in humans as it does in mice. Sinclair, however, has a considerable financial stake in his claims being proven correct, and has lent his scientific prowess to commercializing possible life extension products such as molecules known as "NAD boosters."

His [financial interests](#) include being listed as an inventor on a patent licensed to Elysium Health, a supplement company that sells a NAD booster in pills for \$60 a bottle. He's also an investor in InsideTracker, the company that he says measured his age.

Discerning hype from reality in the longevity field has become tougher than ever as reputable scientists such as Sinclair and pre-eminent institutions like Harvard align themselves with promising but unproven interventions—and at times promote and profit from them.

Fueling the excitement, investors pour billions of dollars into the field even as many of the products already on the market face fewer regulations and therefore a lower threshold of proof.

"If you say you're a terrific scientist and you have a treatment for aging, it gets a lot of attention," said Jeffrey Flier, a former Harvard Medical School dean who has been critical of the hype. "There is financial incentive and inducement to overpromise before all the research is in."

Elysium, co-founded in 2014 by a prominent MIT scientist to commercialize the molecule nicotinamide riboside, a type of NAD

booster, highlights its "exclusive" licensing agreement with Harvard and the Mayo Clinic and Sinclair's role as an inventor. According to the company's press release, the agreement is aimed at supplements that slow "aging and age-related diseases."

Further adding scientific gravitas to its brand, the website lists eight Nobel laureates and 19 other prominent scientists who sit on its scientific advisory board. The company also advertises research partnerships with Harvard and U.K. universities Cambridge and Oxford.

Some scientists and institutions have grown uneasy with such ties. Cambridge's Milner Therapeutics Institute announced in 2017 it would receive funding from Elysium, cementing a research "partnership." But after hearing complaints from faculty that the institute was associating itself with an unproven supplement, it quietly decided not to renew the funding or the company's membership to its "innovation" board.

"The sale of nutritional supplements of unproven clinical benefit is commonplace," said Stephen O'Rahilly, the director of Cambridge's Metabolic Research Laboratories who applauded his university for reassessing the arrangement. "What is unusual in this case is the extent to which institutions and individuals from the highest levels of the academy have been co-opted to provide scientific credibility for a product whose benefits to human health are unproven."

A generation ago, scientists often ignored or debunked claims of a "fountain of youth" pill.

"Until about the early 1990s, it was kind of laughable that you could develop a pill that would slow aging," said Richard Miller, a biogerontologist at the University of Michigan who heads one of three labs funded by the National Institutes of Health to test such promising substances on mice. "It was sort of a science fiction trope. Recent

research has shown that pessimism is wrong."

Mice given molecules such as rapamycin live as much as 20 percent longer. Other substances such as 17 alpha estradiol and the diabetes drug Acarbose have been shown to be just as effective—in mouse studies. Not only do mice live longer, but, depending on the substance, they avoid cancers, heart ailments and cognitive problems.

But human metabolism is different from that of rodents. And our existence is unlike a mouse's life in a cage. What is theoretically possible in the future remains unproven in humans and not ready for sale, experts say.

History is replete with examples of cures that worked on mice but not in people. Multiple drugs, for instance, have been effective at targeting an Alzheimer's-like disease in mice yet have failed in humans.

"None of this is ready for prime time. The bottom line is I don't try any of these things," said Felipe Sierra, the director of the division of aging biology at the National Institute on Aging at NIH. "Why don't I? Because I'm not a mouse."

Concerns about whether [animal research](#) could translate into human therapy have not stopped scientists from racing into the market, launching startups or lining up investors. Some true believers, including researchers and investors, are taking the substances themselves while promoting them as the next big thing in aging.

"While the buzz encourages investment in worthwhile research, scientists should avoid hyping specific (substances)," said S. Jay Olshansky, a professor who specializes in aging at the School of Public Health at the University of Illinois at Chicago.

Yet some scientific findings are exaggerated to help commercialize them before clinical trials in humans demonstrate both safety and efficacy, he said.

"It's a great gig if you can convince people to send money and use it to pay exorbitant salaries and do it for 20 years and make claims for 10," Olshansky said. "You've lived the high life and get investors by whipping up excitement and saying the benefits will come sooner than they really are."

Promising findings in animal studies have stirred much of this enthusiasm.

Research by Sinclair and others helped spark interest in resveratrol, an ingredient in red wine, for its potential anti-aging properties. In 2004, Sinclair co-founded a company, Sirtris, to test resveratrol's potential benefits and declared in an interview with the journal *Science* it was "as close to a miraculous molecule as you can find." GlaxoSmithKline bought the company in 2008 for \$720 million. By the time Glaxo halted the research in 2010 because of underwhelming results with possible side effects, Sinclair had already received \$8 million from the sale, according to Securities and Exchange Commission documents. He also had earned \$297,000 a year in consulting fees from the company, according to *The Wall Street Journal*.

At the height of the buzz, Sinclair accepted a paid position with Shaklee, which sold a product made out of resveratrol. But he resigned after *The Wall Street Journal* highlighted positive comments he made about the product that the company had posted online. He said he never gave Shaklee permission to use his statements for marketing.

Sinclair practices what he preaches—or promotes. On his LinkedIn bio and in media interviews, he describes how he now regularly takes

resveratrol; the diabetes drug metformin, which holds promise in slowing aging; and nicotinamide mononucleotide, a substance known as NMN that his own research showed rejuvenated mice.

Of that study, he said in a video produced by Harvard that it "sets the stage for new medicines that will be able to restore blood flow in organs that have lost it, either through a heart attack, a stroke or even in patients with dementia."

In an interview with KHN, Sinclair said he's not recommending that others take those substances.

"I'm not claiming I'm actually younger. I'm just giving people the facts," he said, adding that he's sharing the test results from InsideTracker's blood tests, which calculate [biological age](#) based on biomarkers in the blood. "They said I was 58, and then one or two blood tests later they said I was 31.4."

InsideTracker sells an online age-tracking package to consumers for up to about \$600. The company's website highlights Sinclair's support for the company as a member of its scientific advisory board. It also touts a study that describes the benefits of such tracking, which Sinclair co-authored.

Sinclair is involved either as a founder, an investor, an equity holder, a consultant or a board member with 28 companies, according to a list of his financial interests. At least 18 are involved in anti-aging in some way, including studying or commercializing NAD boosters. The interests range from longevity research startups aimed at humans and even pets to developing a product for a French skin care company to advising a longevity investment fund. He's also an inventor named in the patent licensed by Harvard and the Mayo Clinic to Elysium, and one of his companies, MetroBiotech, has filed a patent related to nicotinamide

mononucleotide, which he says he takes himself.

Sinclair and Harvard declined to release details on how much money he—or the university—is generating from these disclosed outside financial interests. Sinclair estimated in a 2017 interview with Australia's Financial Review that he raises \$3 million a year to fund his Harvard lab.

Liberty Biosecurity, a company he co-founded, estimated in Sinclair's online bio that he has been involved in ventures that "have attracted more than a billion dollars in investment." When KHN asked him to detail the characterization, he said it was inaccurate, without elaborating, and the comments later disappeared from the website.

Sinclair cited confidentiality agreements for not disclosing his earnings, but he added that "most of this income has been reinvested into companies developing breakthrough medicines, used to help my lab, or donated to nonprofits." He said he did not know how much he stood to make off the Elysium patent, saying Harvard negotiated the agreement.

Harvard declined to release Sinclair's conflict-of-interest statements, which university policy requires faculty at the medical school to file in order to "protect against any faculty bias that could heighten the risk of harm to human research participants or recipients of products resulting from such research."

"We can only be proud of our collaborations if we can represent confidently that such relationships enhance, and do not detract from, the appropriateness and reliability of our work," the policy states.

Elysium advertises both Harvard's and Sinclair's ties to its company. It was co-founded by Massachusetts Institute of Technology professor Leonard Guarente, Sinclair's former research adviser and an investor in Sinclair's Sirtris.

Echoing his earlier statements on resveratrol, Sinclair is quoted on Elysium's website as describing NAD boosters as "one of the most important molecules for life."

The Food and Drug Administration doesn't categorize aging as a disease, which means potential medicines aimed at longevity generally can't undergo traditional clinical trials aimed at testing their effects on human aging. In addition, the FDA does not require supplements to undergo the same safety or efficacy testing as pharmaceuticals.

The banner headline on Elysium's website said that "clinical trial results prove safety and efficacy" of its supplement, Basis, which contains the molecule nicotinamide riboside and pterostilbene. But the company's research did not demonstrate the supplement was effective at anti-aging in humans, as it may be in mice. It simply showed the pill increased the levels of the substance in blood cells.

"Elysium is selling pills to people online with the assertion that the pills are 'clinically proven'" said O'Rahilly. "Thus far, however the benefits and risks of this change in chemistry in humans is unknown."

"Many interventions that seem sensible on the basis of research in animals turn out to have unexpected effects in man," he added, citing a large clinical trial of beta carotene that showed it increased rather than decreased the risk of lung cancer in smokers.

Elysium's own research documented a "small but significant increase in cholesterol," but added more studies were needed to determine whether the changes were "real or due to chance." One independent study has suggested that a component of NAD may influence the growth of some cancers, but researchers involved in the study warned it was too early to know.



Guarente, Elysium's co-founder and chief scientist, told KHN he isn't worried about any side effects from Basis, and he emphasized that his company is dedicated to conducting solid research. He said his company monitors customers' safety reports and advises customers with health issues to consult with their doctors before using it.

If a substance meets the FDA's definition of a supplement and is advertised that way, then the agency can't take action unless it proves a danger, said Alta Charo, a former bioethics policy adviser to the Obama administration. Pharmaceuticals must demonstrate safety and efficacy before being marketed.

"A lot of what goes on here is really, really careful phrasing for what you say the thing is for," said Charo, a law professor at the University of Wisconsin. "If they're marketing it as a cure for a disease, then they get in trouble with the FDA. If they're marketing it as a rejuvenator, then the FDA is hamstrung until a danger to the public is proven."

"This is a recipe for some really unfortunate problems down the road," Charo added. "We may be lucky and it may turn out that a lot of this stuff turns out to be benignly useless. But for all we know, it'll be dangerous."

The debate about the risks and benefits of substances that have yet to be proven to work in humans has triggered a debate over whether research institutions are scrutinizing the financial interests and involvement of their faculty—or the institution itself—closely enough. It remains to be seen whether Cambridge's decision not to renew its partnership will prompt others to rethink such ties.

Flier, the former dean of Harvard Medical School, had earlier heard complaints and looked into the relationships between scientists and Elysium after he stepped down as dean. He said he discovered that many

of the board members who allowed their names and pictures to be posted on the company website knew little about the scientific basis for use of the company's supplement.

Flier recalls that one scientist had no real role in advising the company and never attended a company meeting. Even so, Elysium was paying him for his role on the board, Flier said.

Caroline Perry, director of communications for Harvard's Office of Technology Development, said agreements such as Harvard's acceptance of research funds from Elysium comply with university policies and "protect the traditional academic independence of the researchers."

Harvard "enters into research agreements with corporate partners who express a commitment to advancing science by supporting research led by Harvard faculty," Perry added.

Like Harvard, the Mayo Clinic refused to release details on how much money it would make off the Elysium licensing agreement. Mayo and Harvard engaged in "substantial diligence and extended negotiations" before entering into the agreement, said a Mayo spokeswoman.

"The company provided convincing proof that they are committed to developing products supported by scientific evidence," said the spokeswoman, Duska Anastasijevic.

Guarente of Elysium refused to say how much he or Elysium was earning off the sale of the supplement Basis. MIT would not release his conflict-of-interest statements.

Private investment funds, meanwhile, continue to pour into longevity research despite questions about whether the substances work in people.

One key Elysium investor is the Morningside Group, a private equity firm run by Harvard's top donor, Gerald Chan, who also gave \$350 million to the Harvard School of Public Health.

Billionaire and WeWork co-founder Adam Neumann has invested in Sinclair's Life Biosciences.

An investment firm led by engineer and physician Peter Diamandis gave a group of Harvard researchers \$5.5 million for their startup company after their research was publicly challenged by several other scientists.

In its announcement of the seed money, the company, Elevian, said its goal was to develop "new medicines" that increase the activity levels of the hormone GDF11 "to potentially prevent and treat age-related diseases."

It described research by its founders, which include Harvard's Amy Wagers and Richard Lee, as demonstrating that "replenishing a single circulating factor, GDF11, in old animals mirrors the effects of young blood, repairing the heart, brain, muscle and other tissues."

Other respected labs in the field have either failed to replicate or contradict key elements of their observations.

Elevian's CEO, Mark Allen, said the early [scientific data](#) on GDF11 is encouraging, but "drug discovery and development is a time-intensive, risky, regulated process requiring many years of research, preclinical (animal) studies, and human clinical trials to successfully bring new drugs to market."

Flier worries research in the longevity field could be compromised, although he recognizes the importance and promise of the science. He said he's concerned that alliances between billionaires and scientists

could lead to less skepticism.

"A susceptible billionaire meets a very good salesman scientist who looks him deeply in the eyes and says, 'There's no reason why we can't have a therapy that will let you live 400 or 600 years,'" Flier said. "The billionaire will look back and see someone who is at MIT or Harvard and say, 'Show me what you can do.'"

Despite concerns about the hype, scientists are hopeful of finding a way forward by relying on hard evidence. The consensus: A pill is on the horizon. It's just a matter of time—and solid research.

"If you want to make money, hiring a sales rep to push something that hasn't been tested is a really great strategy," said Miller, who is testing substances on mice. "If instead you want to find drugs that work in people, you take a very different approach. It doesn't involve sales pitches. It involves the long, laborious, slogging process of actually doing research."

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