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How I Did It

Inspiration and insights from the founders of

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SHARK TANK'S
DAYMOND JOHN

"People allow
me to invest in
their dreams."

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GUIDE TO
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BY **JEFF
BERCOVICI**
PHOTOGRAPH BY
JAMIE CHUNG

**They're trying to beat
Alzheimer's, cure viral diseases,
and kill tumors with gold.**

**One common thread:
funding from Peter Thiel**

IN 2010, BRIAN FREZZA AND D.J. Kleinbaum were four hours from leaving Silicon Valley for good. Since childhood, the two best friends had been incubating a shared dream of using computer science to cure diseases. They had first pitched investors on their vision six years earlier, as seniors studying computational biology at Carnegie Mellon University, but the door hit them on their way out of every meeting. "No one will fund you or let you run a biotech company without three letters after your name," Kleinbaum says.

So, after graduation, the pair left Pittsburgh to acquire those formal creds. Kleinbaum enrolled in a PhD program at Stanford while Frezza went to Scripps Research Institute in San Diego. In June 2010, days before Frezza was supposed to defend his thesis, he told his adviser he had bigger ambitions than academia. "He was livid," Frezza recalls. "He had kind of assumed I was going to be his protégé."

For years the duo had been scrawling code for a robotic biochemistry lab that would run experiments radically faster than had ever before been possible. They were about to file their first patent applications for "bioorganic

FIXING PHARMA

Computational biologists Brian Frezza (left) and D.J. Kleinbaum are developing nanotechnology that could cure AIDS.

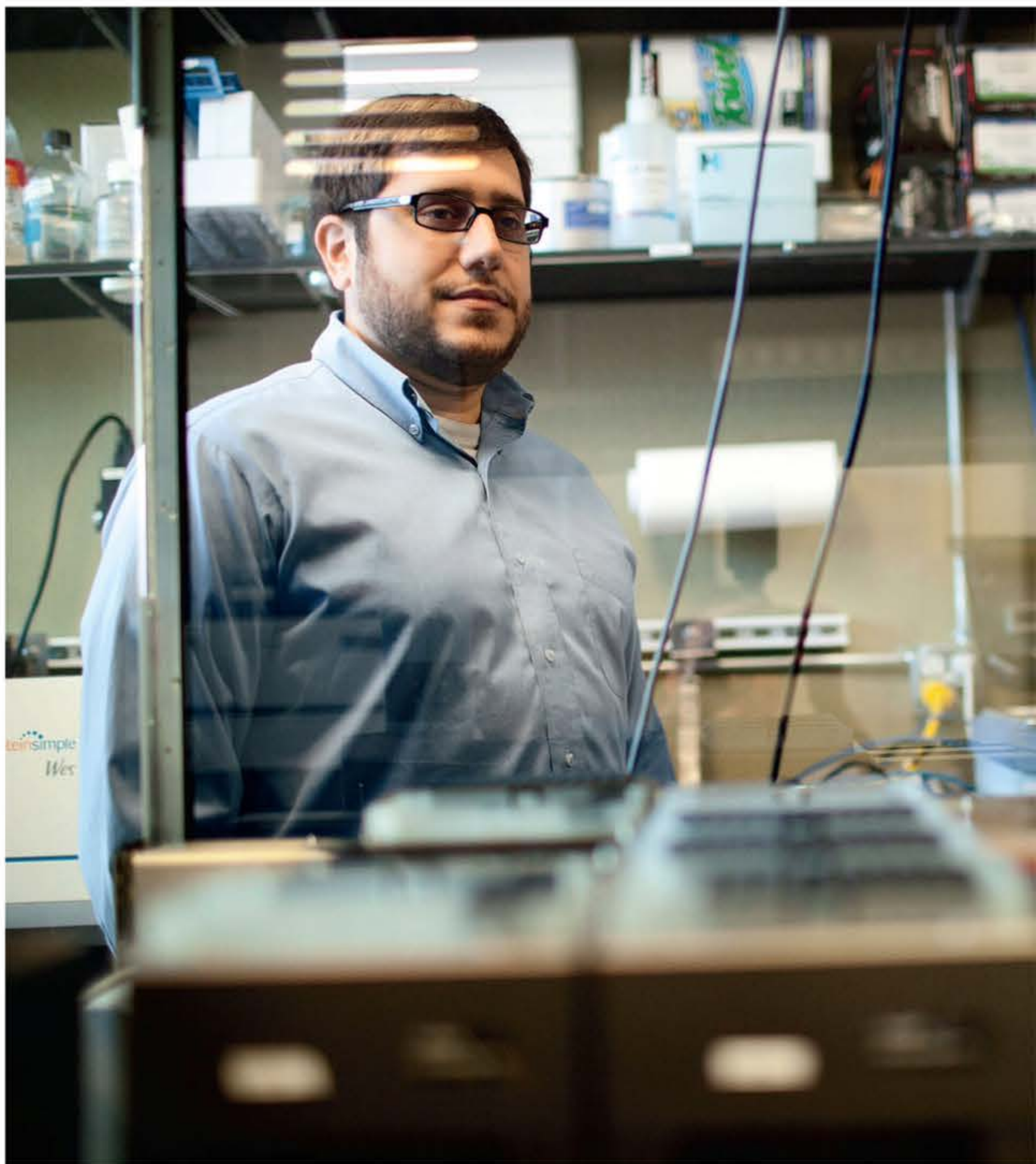
nanotechnology,” the theoretical basis of a novel class of drugs that would, they believed, yield a cure for AIDS and other persistent viral infections. (If that sounds vague, it’s supposed to; the healthily paranoid Frezza says they’re still a year away from being ready to talk about it.) Incensed by his adviser, Frezza put off his thesis, packed up his car, drove eight hours north to Palo Alto, and camped out on Kleinbaum’s couch so they could find the funding that would finally make their company a reality.

It was a distinctly lousy time to be raising cash for a startup like theirs. Two years earlier, venture capital investment in biotech had plunged by more than one-third, and it hadn’t stirred since. Unlike software plays, biotech startups are particularly high risk and capital intensive, with nebulous, sprawling timelines. Now, six years after that initial round of rejection, the more credentialed pair were disappointed to find themselves receiving the same chilly reception. Nobody wanted to make a big bet on two twentysomethings with no track record doing wet-lab work. “I’ve lost track of how many VC firms I’ve been asked to leave, either politely or impolitely,” says Kleinbaum.

They had resigned themselves to returning to Pittsburgh, where they had wrangled some angel funding and lab space. But before leaving town, they played their last card. PayPal co-founder Max Levchin was the former boss of Frezza’s older brother, who died in 2001 of complications from type 1 diabetes. Levchin spoke at the funeral and over the years had become an informal mentor to Frezza. After Frezza called him with his and Kleinbaum’s plans, Levchin

offered them seed money, and something even more valuable—an invitation to connect with his PayPal co-founder, Peter Thiel, one of the few VCs, according to Levchin, prepared to “make extreme bets on stuff that sounds right out of a science-fiction novel.”

A few days later, four hours before they were scheduled to embark on the demoralizing road trip back east, Frezza and Kleinbaum walked into Thiel’s Founders Fund office. As Facebook’s first outside investor and a serial entrepreneur, Thiel had amassed a net worth of more than \$2 billion. Lately, however, he had begun feeling that the apportionment of venture capital in Silicon Valley was out of whack, with too much of it going to software companies, like



“I’VE LOST TRACK OF HOW MANY VC FIRMS I’VE BEEN ASKED TO LEAVE.”

—D.J. KLEINBAUM

SPREAD: CLOCKWISE FROM TOP: TIM HUSSIN/AP; BERLINER/AP; STEVE JENNINGS/CETV; SETH WENG/AP; NUSHMIA KHAN; KIM KILSH/AP



the ones that made him rich, and not enough to startups tackling knotty scientific challenges. Using robots and nanotechnology to cure AIDS was just the sort of audacious, potentially world-changing idea he wanted to fuel.

Half an hour into their pitch, Thiel urged Frezza and Kleinbaum to postpone their departure a week so he could persuade them to stay indefinitely in the Bay Area. "They'd been in [academia] long enough to prove they were really good at it, but they hadn't been in it so long that they had completely given up all hope," says Thiel. The pair camped out in motels and worked out of a laundromat with Wi-Fi. One week of bohemian living turned into several months—albeit the most life-altering

months of their lives. By the time winter came around, Emerald Therapeutics, as they'd named their company, had its first Series A investment from Founders Fund, and Frezza soon finished his PhD. Thiel, meanwhile, had a new crusade, which also happened to be a very old one.



PETER THIEL can identify the moment he learned life had an expiration date. He was all of 3 years old, lying on a cowhide

rug on the floor of his family's apartment in Cleveland, when he asked his father, Klaus, what had become of the cow. "It was really, really disturbing," Thiel recalls of trying to wrap his mind around death. "I somehow never lost that sense of being disturbed about it."

By the time he arrived at Stanford in the late 1980s, he was still so captivated by the "problem" of nonbeing (see "Funding Immortality," right) he considered majoring in genetic engineering. But impatience got in the way. "Life sciences, unlike computer sciences, is this field where you historically have needed a far longer set of credentials, 10 or 15 years of training, before you can really start interesting research or for-profit work," he says. So he fast-tracked with a philosophy degree, a law degree, and the foresight to start PayPal by the time he was 31.

In 2008, Thiel made Founders Fund's first substantial biotech investment, in genomics company Halcyon Molecular. It was a counterintuitive moment for the three-year-old firm to go bullish in biotech. The financial crisis along with new federal regulations had sent the sector off a precipice. IT startups, which can bring a "minimum viable product" to market in weeks—versus the years or decades required for drugs and therapeutics—had become the more seductive option for investors. Even venture firms that specialized in biotech were migrating toward "digital health" outfits that worked with bits, not cells. According to the National Venture Capital Association, venture spending on biotech fell from \$6 billion in 2007 to \$3.9 billion in 2009 (not until 2014 did it regain its previous level). Meanwhile, Thiel believed biotech was

FUNDING IMMORTALITY

If anyone has the cash (and hubris) to reduce death to a problem simply waiting to be solved, it's the entrepreneurs who have made their fortunes doing the seemingly impossible. These five tech titans are bankrolling attempts to outsmart mortality.

LARRY ELLISON



One of the world's richest men, with a personal net worth of \$55 billion, the Oracle co-founder is used to getting his way, and he doesn't see why that should ever stop. "Death makes me very angry," he has said, explaining why he has spent hundreds of millions to fund antiaging research. Although his biomedical foundation shifted its focus in 2013, he remains an investor in genomics pioneer Craig Venter's startup, Human Longevity.

LARRY PAGE AND SERGEY BRIN



Google's co-founders are pursuing multiple routes to defy mortality: In 2013, they launched Calico, a Google subsidiary focused on "curing death."



Google is also the new home to Ray Kurzweil, a leading theorist of human immortality. Brin (bottom), who carries a gene mutation that puts him at elevated risk for developing Parkinson's disease, has donated \$150 million to researching a cure.

BRYAN JOHNSON



In 2014, the Braintree founder earmarked \$100 million to start OS Fund, an investment vehicle for pursuing "quantum-leap" science, which includes both "curing aging" and "re-creat[ing] the biological tool set of our existence." Johnson was the first outside investor in Venter's Human Longevity, which aims to stretch the average human lifespan to 120 years.

PETER THIEL



Before he started investing in biotech startups, the PayPal co-founder and venture capitalist was sponsoring the longevity studies of the SENS Research Foundation, run by controversial British antiager Aubrey de Grey. Thiel believes the acceptance of death is a psychological defense mechanism and dismisses as "weird and sociopathic" the arguments that longer lifespans might worsen overpopulation or economic inequality. "Even if there are some problems with it," says Thiel, "it's better than being dead."

BIOTECH'S UNICORN

Thiel's Founders Fund invested \$17 million in Ramji Srinivasan's Counsyl, a genetic testing startup now valued at more than \$1 billion.

on the cusp of a revolution. Innovations like 3-D printing, virtualization, and automation were reducing the cost of experimentation, while powerful algorithms were making it possible to extract insights from the human genome in hours, not weeks.

Halcyon Molecular set out to cure all diseases for under \$100 a pop by decoding the entire human genome. However, Founders Fund soon learned there was such a thing as an overly ambitious biotech bet, a \$10 million lesson that would shape the firm's investment strategy. In 2012, a U.K.-based competitor claimed to have solved the problem Halcyon was still working to crack, so the founders abruptly shut down their company (though they later found out the claim was premature). In retrospect, Thiel realized that setting out to solve every medical problem was a red flag for biotech startups. "You want to avoid things that feel too much like a Rube Goldberg, where you have to get a vast number of things to work," says Thiel.

Fortunately, in 2011 Founders Fund had invested in another company pursuing cheap genetic testing, only this one was sharply focused. San Francisco-based Counsyl homed in on a small number of heritable disorders about which the science was straightforward. "The unconventional thing there was being more pessimistic about what you could do with genomics," says Thiel of his firm's \$17 million investment. The startup supplements testing with counseling services to help patients—largely expectant parents—understand the results. "A lot of companies do genomics for the sake of genomics," says Ramji Srinivasan, Counsyl's CEO. "Our value isn't in that. Customers don't buy technology; they buy something that solves their needs."

Now worth more than \$1 billion, Counsyl has 330 employees and contracts with insurers covering some 150 million people. Srinivasan says the speed with

which companies like his are able to innovate makes them attractive vehicles for the sort of impatient entrepreneurial types who shied away from biotech in the past. "I don't think people appreciate how messy biology is compared with computer science," he says. "Now we have the tools where we can literally hire scientists and credibly tell them they're going to work on things that will impact patients today, tomorrow, next week, instead of 10 years from now."

Matthew Scholz is exactly the sort of computer scientist who wouldn't have had much interest in the pace of conventional medical science. In 2008, he was running a software company that managed logistics for urban delivery fleets. While preparing to sell his startup, he began noodling on the similarities between cybersecurity techniques and the processes of the human immune system. "I just assumed, gosh, since the body is just basically information, surely people have been programming cells," he says. "It was naiveté leading me down a path that turned out to be very fruitful."

By 2009, Scholz had recruited biologists and bootstrapped Immusoft, which "programs" B cells—types of white blood cells that produce antibodies—to generate their own medicine. The concept: Instead of injecting treatments into a

"PEOPLE DON'T APPRECIATE HOW MESSY BIOLOGY IS COMPARED WITH COMPUTER SCIENCE."

—RAMJI SRINIVASAN

patient, cells are extracted, rewired to produce a treatment, and then returned to the body. At the time, no cell therapy using gene modification had ever won regulatory approval. (This was years before similar startups like Juno Therapeutics and Editas Medicine were raising tens of millions of dollars.) With \$2.3 million from Founders Fund and other investors, the company is now preparing for its first human trials. If they come to market, long-lasting DNA therapies like Immusoft's could become a giant thorn for pharma companies whose profits depend on eternal prescription refills. "Once we treat all their patients, they're done," says Scholz.

"The thesis that biotech starts to look more like engineering disciplines is the one that makes us feel good about the investments we've made," says

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Scott Nolan, one of Founders Fund's partners. In addition to Counsyl, Emerald, and Immusoft, those investments include Cambrian Genomics, a maker of DNA-printing technology, and Stemcentrx, which is working on a new therapy for solid tumors.

But even Founders Fund recognized its limits when it came to taking risks in biotech. When you're gambling in the revolutionary instead of the incremental, "it's always this big chicken-and-egg problem," explains Thiel. Investors want to put money into a company only after it has shown at least a hint of traction, but proving that new science has real-world applications requires hefty capital. This double-bind is why most science research still happens within the confines of universities.

In 2011, Thiel's colleague Lindy Fishburne proposed a way out of this impasse. A senior vice president at the Thiel Foundation—whose mission is to advance "political, personal, and economic freedom"—Fishburne was equally frustrated that venture capital was running away from all but the safest bets in biotech. "You had all this interesting work percolating and absolutely no capital there to catch it," Fishburne says. "I made this argument to Peter that philanthropy is supposed to jump in where markets are broken. Well, the market was broken around funding innovation, particularly at the intersection of biology and technology."

The result was Breakout Labs, which turbocharges breakthrough science happening primarily in aca-

demia. Breakout finds teams at universities that have gone as far as they can go with grants and, in Thielian jargon, "jailbreaks" them with \$350,000 in seed funding. That initial cash infusion converts into equity if the new company succeeds in obtaining additional funding, but behaves like a grant if it doesn't. "We're really focused on jumping out of the lab and into the economy," Fishburne says.

The model intends to deliver benefits to all: Universities get to license technologies developed under their roof; the government can see the grants it doles out transcend medical journals; and the startups get more juice to become viable companies. The team behind one Breakout-funded startup, EpiBone, had taken \$10 million in federal grant money for the company's research on growing replacement

"WE'RE FOCUSED ON JUMPING OUT OF THE LAB AND INTO THE ECONOMY."

—LINDY FISHBURNE

bones in labs. Last fall, it secured \$4.2 million in additional funding, including an investment from City of New York Early-Stage Life Sciences Funding Initiative. Although promising, EpiBone's technology is still being tested on pigs. "If we're lucky, it will be about eight years to market," concedes CEO Nina Tandon on the realities of her field.

Other Breakout companies are working on ways to flash-freeze organs for better transplantation outcomes (Arigos Biomedical), kill tumors with gold nanoparticles (Siva Therapeutics), and grow meat and leather from cultured animal cells (Modern Meadow). A startup called Cortexyme has particularly captured Thiel's imagination. Casey Lynch, its co-founder and CEO, is working to debunk the prevailing belief that Alzheimer's disease is caused by a buildup of misshapen protein fragments

in the brain, and to advance the hypothesis that it results from a bacterial infection. Though her provocative therapy is still several years away from a human trial, it's shown astonishing results in mice. For the immortality-obsessed Thiel, curing a disease that afflicts one in three people who live past 85 is "the biggest single thing we could be working on, full stop."

But of all Thiel's investments, Emerald Therapeutics perhaps has the most potential to help accelerate the next biotech revolution. Instead of just trying to develop new drugs, the entrepreneurs also want to fix the costly structural problems that have made the industry so bad at developing them. In March, Frezza and Kleinbaum opened the Emerald Cloud Lab, a robotic facility in South San Francisco where the startup is making its automation tech-

nology available to other startups for an average fee of \$20 per experimental sample. Researchers can run more than 40 biochemistry experiments remotely, programming them in via the Web. Just as Amazon Web Services unleashed a frenzy of entrepreneurship by eliminating the need for software startups to buy their own servers, the co-founders think they can spur innovation in life sciences by offering virtual lab space to small teams working anywhere around the globe. Thanks to the Cloud Lab, the next wonder drug may not be designed in a university lab but in a dorm room across campus. Trying to cure a disease is a noble goal; making it easier for anyone to cure any disease—that's a game-changing one. **1**

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