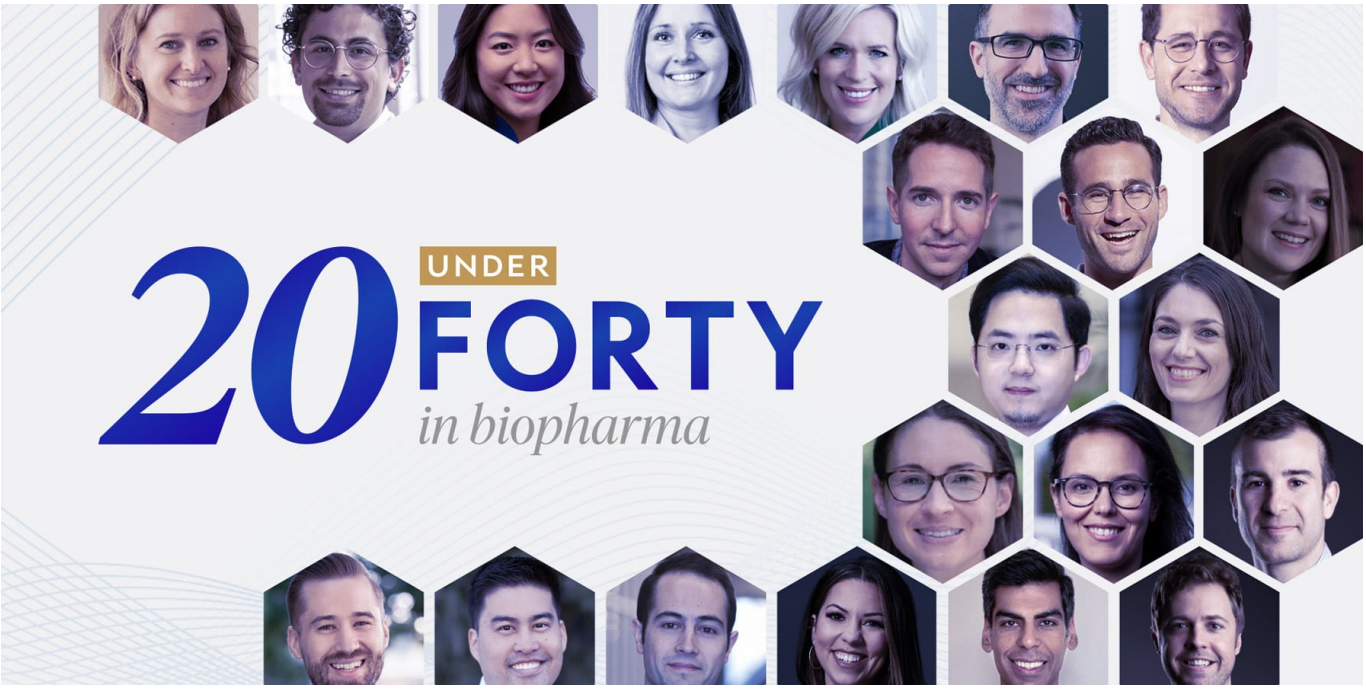
ENDPOINTS NEWS

# The 20(+1) under 40: Inside the next generation of biotech leaders

by **Endpoints Staff** on April 6th, 2021




How does one decide who makes an "under 40" list? After the last nominations come in from staff and readers, we're left to sort through hundreds of names, with no obvious guideposts for how to do so. Do we want the basic scientist behind a major discovery, or the executive working to translate it into medicines? The venture capitalist spinning out a half-dozen companies or the founder with one big idea? Leaders who have already brought drugs into the clinic or leaders who seem on the cusp of it?

Ultimately, we're left with no hard-and-fast rules except that they have to be under 40 — and at least a few would-be names turned out to be just over — and that their stories are crucial to understanding the industry today. Perhaps their work, if it succeeds, would change medicine. Or perhaps they're beginning to push the industry, which can sometimes cater to the grey-haired and pedigreed, into new areas, bringing new technologies to untested scientific terrain and proposing new ways to think about old problems.

This year, *Endpoints News* has brought you leaders and thinkers with ambitious ideas from around the world and across a motley of cutting edge fields, people who could one day become household names: the CEO trying to resurrect psychedelics for depression and PTSD; the academic-turned-founder chasing the most notorious disease in drug development; the professor's son attempting to build a Covid-19 vaccine for the world.

In some cases, we decided that honoring just one person wasn't enough. Science is an inextricably collaborative effort and as we reported, we realized that some people's stories couldn't be told without the story of the other young scientist working beside them. So for the first time, we've included two dual profiles and, as a result, a 20-under-40 list that contains 21 people.

It's a bit odd, we'll admit, but they're two of the best stories in the project — stories of what two quick, hungry minds can do when brought together at the right moment. You won't want to miss them or any of the others. And unlike the last two years, we've included video snippets from each of the interviews, to really give a sense of who they are.

— *Jason Mast*

The Endpoints 20 under 40, 2021

- Ranjan Batra
- Florian Brand
- Mark Chao
- Emily Drabant Conley
- Leen Kawas
- Juliette Hordeaux
- Eric Kelsic
- Mike Klichinsky
- Alexis Komor & Nicole Gaudelli
- Marc Lajoie & Scott Boyken
- Joshua Liang
- Sean McClain
- Ben Oakes
- Imogen Pryce
- Glenn Rockman
- Jake Rubens
- Carol Suh
- Christina Trojel-Hansen
- Laura Walker

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- Name **Ranjan Batra**
- Company **Locanabio**
- Position **VP of R&D**
- Age **38**

**Bringing a pharmacist's eye to RNA, Ranjan Batra tries to do for Huntington's what Zolgensma did for SMA**

Ranjan Batra remembers seeing Jennifer Doudna at a scientific conference in Seattle.

She wasn't talking about CRISPR/Cas9, the gene editing tool that would eventually win her the Nobel Prize in chemistry. Back in 2010, Doudna was known chiefly as one of the world's more prominent RNA experts alongside Melissa Moore, who would go on to become CSO of platform research at Moderna. There weren't many of them.

"RNA Society meetings were a lot less crowded," he recalled. "So the community was really small, it was academic, it wasn't really about treatments mediated at the level of RNA, it was more about — a lot about discovery, a lot about biomarkers."

Batra himself was new to the field, having been introduced by Maurice Swanson, his principal investigator and PhD advisor at the University of Florida. It was his first degree in genetics — a field he stumbled upon while doing a master's in pharmacology — and the initial step toward a career in CRISPR.

The fascination with drugs and the human body, though, began early.

Growing up in New Delhi, he shared a love of biology with his mother and pondered what's going on in the excretory system or the brain. He recalled reading the publications that his pharmacist father would bring home — specifically, he recalled reading a book around sixth grade and feeling mind blown by an article stating that aspirin, which has been in use for more than a century, came from willow bark.

"That was really exciting to me, I was just thinking how these chemicals kind of grow in your body and just cause an effect, or relieve you of different symptoms," he said.

At that point, it was still proteins he was thinking about. But as he learned more about DNA, plasmids, and other genetic constructs at Swanson's lab, he began looking at diseases from the RNA perspective — in particular, modeling RNA-mediated diseases like myotonic dystrophy and familial amyotrophic lateral sclerosis.

The pharmacist in him began to wonder about molecules that bind RNA, which was why he eventually went to UC-San Diego to do a postdoc with Gene Yeo — whose expertise spans both bioinformatics and RNA-binding proteins — after meeting him at another RNA Society meeting.

At UCSD, he struck up a quick friendship with Dave Nelles, a graduate student who had collaborated with the Doudna lab to show that CRISPR/Cas9, the system famous for editing DNA, could actually be modified to target RNA. There was just one hurdle for turning that into a therapeutic approach: the whole complex, complete with Cas9 and a guide RNA engineered with a synthetic oligonucleotide, was too big to be packaged into a single AAV and had to be co-delivered in two separate vectors.

So he worked with Nelles to tweak the system in a way that wouldn't require the oligomer, by hitting

repetitive RNA structures behind a specific group of diseases. Diseases, as it turned out, like myotonic dystrophy, with models Batra had developed and could easily access.

“That was, I would say, the fastest study that I’ve ever done. and the fastest paper that I’ve written,” he said. “But like it’s the biggest paper and the biggest data I’ve ever generated.”

He published the paper in eight months and then moved on, toying with immuno-oncology at Verily, mostly to satisfy a curiosity in what Google was doing in life sciences, before he heard again from Yeo and Nelles. They had spun out a new company called Locanabio, and they wanted him to run the preclinical work.

“Ron is tremendously thoughtful,” Yeo said. “He does deep due diligence on the feasibility and utility of a particular therapeutic strategy and its fit to a disease. And I think that blend between understanding diseases and knowing what is needed to model them and then to measure and, if you can, see reversal of a phenotype upon treatment of a therapeutic, it’s important.”

Now VP of R&D at LocanaBio, Batra is slowly pushing for once-and-done therapies that can do for myotonic dystrophy, Huntington’s and other ailments what Zolgensma did for spinal muscular atrophy. While he’s now immersed in other aspects of a biotech startup, he still finds the time to get on the bench when possible, recently performing RNA isolation from a brain sample followed by digital droplet PCR to quantify expression and target engagement of Locana’s therapeutic candidates.

The kind of rigor that he was introduced to during those early days studying RNA biology is still evident, extending to dreams like having better deep learning models that would allow scientists to revisit non-human primate studies and thereby challenging some long-held assumptions in biomedical research. But he’s open to more pivots.

“I like to do science for an end goal,” he said. “In this case it’s therapeutics, someday I hope that I’m doing science for like climate change, I don’t know.” — *Amber Tong*

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- Name **Florian Brand**
- Company **ATAI Life Sciences**
- Position **CEO**
- Age **34**

**After discovering the power of psychedelics, Florian Brand 'followed the evidence' to a Peter Thiel-backed startup**

How does one go from selling kitchen appliances to running a Peter Thiel-backed psychedelics startup? A lot of serendipity, Florian Brand says.

Brand was born in Hamburg, Germany and spent most of his teenage years in Frankfurt, where he experienced severe anxiety for the first time. Luckily, with the help of a great therapist, psychotherapy worked for him. He went on to study economics at Ludwig Maximilian University in Munich, and did a master's program in management at ESCP Europe.

In 2013**,** he and a good friend, Lars Christian Wilde, launched Springlane GmbH — a company that "basically brought the Williams-Sonoma concept in an online-first approach to Europe," Brand said. The concept was a recipe sharing platform, which would inspire foodies to buy their products, which range from mixers to pasta machines.

A few years in, Wilde developed severe anxiety and depression. He tried selective serotonin reuptake inhibitors (SSRIs), and "the whole rigmarole of psychiatric care," he said. But nothing worked.

"That was the first time where I saw someone really being failed ... by the mental health care system," Brand said.

That's when Christian Angermayer, one of their investors, pointed Wilde to a Johns Hopkins and Imperial College study which showed "really large effect size" of psilocybin — the substance in "magic mushrooms" — in patients with anxiety and depression. After doing his own research, Wilde ended up trying a high-dose psychedelic. It worked.

"For me, it was really this miraculous one-and-done experience with it," Wilde said.

In 2016, Wilde launched Compass Pathways with George Goldsmith and Ekaterina Malievskaia to develop psilocybin for therapeutic use. And after realizing the field's broader potential, Brand came on board to help launch ATAI Life Sciences in 2018, a platform company focused on both psychedelic and non-psychedelic treatments for mental health disorders.

"The evidence was compelling, so we basically followed the evidence," Brand said. "But it wasn't ever that I thought 'I want to be a drug developer.'"

ATAI has since raised over $350 million, becoming in the process one of the most prominent private promoters and drivers of psychedelic therapy.

The company — named after Atai, the Efik goddess of creation from African mythology — has four compounds in the clinic so far: for treatment resistant depression, opioid use disorder and generalized anxiety disorder. Back in January, they struck a partnership with Mass General's new Center for Neuroscience of Psychedelics, which seeks to study the mechanisms that underlie the therapeutic effects of psychedelics.

Brand expects to read out Phase IIb results for psilocybin, their lead compound for treatment resistant depression, in Q4 of this year.

“What I’m personally very excited about is figuring out a very elegant way of making those therapies more targeted,” the 34-year-old CEO said. “So right now, it’s often treating the disease, not the patients, and we know that those diseases are very heterogeneous. So you should speak about depressions, not depression, because there are so many different manifestations of those disorders. It really depends on the patient.”

When ATAI first launched, Brand said the company was met with a lot of skepticism from investors. But in November, billionaire entrepreneur Thiel injected $12 million into ATAI’s Series C round, bringing the total raise to $125 million.

“ATAI’s great virtue is to take mental illness as seriously as we should have been taking all illness all along,” he said, per CNBC.

In August**,** ATAI uncloaked EmpathBio — a subsidiary focused on making MDMA-like compounds with a better profile.  EmpathBio CEO Glenn Short has pointed to the potential to tweak the molecules to reduce the risk of drug-related hypertension, allowing it to be given to patients with co-morbidities, as well as allowing it to be given over shorter periods of time and in less controlled settings.

“There’s no stopping him,” Wilde said of Brand. “He has this boundless supply of energy,” adding that he’ll have catch-up calls with the CEO at 2 a.m., only to see him online again at 8 a.m.

“It’s very fulfilling because I’m working on something that is dear to my heart,” Brand said. “Because I saw our friends and family suffer from mental health disease as well as myself, so I actually am privileged to work on something with purpose.” — *Nicole DeFeudis*

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- Name **Mark Chao**
- Company **Gilead**
- Position **VP of Oncology Clinical Research**
- Age **38**

**Forty Seven's golden boy Mark Chao continues the push for new AML therapies at Gilead**

If you ask Stanford stem cell pioneer Irv Weissman about his first impressions of former pupil and Forty Seven colleague Mark Chao, prepare to buckle in.

Weissman, who ran the research lab where Chao worked in med school, has nothing but praise for his ex-student, giving an extended, half-hour long answer to the opening question of his interview with Endpoints. Among the homily's themes included how Chao wasn't a typical med school student and his ability to absorb information from a host of different mentors — the sorts of plaudits one might expect from a professor when discussing their old students.

But what really set Chao apart, Weissman said, was a natural inquisitiveness that led him to question everything rather than take everything at face value. Whereas many medical students end up where they are thanks to a hypercompetitive undergrad career and reliance on memorizing facts from textbooks, Chao stood out by making the change to a "totally evidence-based life" almost immediately after joining Weissman's lab.

"I saw him make that transition right away," Weissman said. "Pretty soon he had read papers I had never even heard of. I knew already he had a really inquiring mind."

It's part of the attitude that helped Chao become one of the key figures at Forty Seven, the CD47-

focused biotech acquired by Gilead last year for nearly $5 billion. And as magrolimab, the crown jewel of the buyout, barrels through development with a breakthrough therapy designation, Weissman credits Chao with much of the biotech's successes.

Chao has always considered himself a curious person, asking the "why" from a young age whenever learning new things. Growing up in northern Virginia, he took a summer job helping with NIH research in high school and learned how to conduct scientific experiments at a basic level.

"The love of thinking and how do you analyze thinking, even at that early age, that's been a core skill set that's helped me throughout my journey," Chao said.

As recently as 10 years ago, when he was still in med school, Chao hadn't considered a career in industry. He had his mind set on what he called a "40-year academic plan" and had mapped out a separate path to faculty around the time Forty Seven was founded in 2014.

But he also knew he wanted to see how his work could impact patients. A pivotal motivation for this came during his third year of med school while doing rotations in a hematological ward, taking care of patients with acute myeloid leukemia. Chao was taken aback by the fact that the therapies for these patients were the same as drugs used 40 years ago.

One particular person stood out to Chao: a 30-year-old mother of three who was "one of the nicest people," he says. This woman spent about a month to a month and a half in the hospital, and by Chao's recollection, never once complained about the aggressive treatments, even when neurotoxic infections popped up. She ended up getting a transplant and fared well for about two years before relapsing while

Chao was a fellow.

Left with few options, the woman, unfortunately, passed away a few months later. The experience helped redouble Chao's focus on developing new treatments and getting back into the lab, he says.

"I remember sitting outside her hospital room with the latest bone marrow results showing that, again, her leukemia was resistant and knowing that we didn't have many options," Chao said, "To not be able to have hope, and provide optionalities as a physician, that still haunts me to this day."

After med school, Chao returned to Stanford and worked in Weissman's lab for his PhD. The duo began asking themselves how they could design better therapies for leukemia and eventually discovered how CD47 plays a role in cancer. Weissman lays much of that work at Chao's feet, noting how Chao took over more and more of the project over time.

Ultimately, they figured out how CD47 acts as a "don't eat me" signal in the immune system, allowing tumors to avoid detection by the first responder-like macrophages in cancer patients. By blocking CD47 then, they reasoned, they could theoretically get immune cells to attack the cancer in the way they're supposed to.

Chao and Weissman's lab group then worked out a way to focus the therapies only on the cancer-expressing cells with CD47 and not healthy cells, eventually spinning Forty Seven out of Stanford. The rest is history — magrolimab proved to be the centerpiece of Gilead's buyout last year, and after earning its BTD, continued reading out positive data in an ongoing Phase Ib study last December in first-line AML.

Making the transition to industry proved another challenge for Chao given his "zero experience" in the area, but Weissman figured he'd still be up to the task. The moment that happened came when Chao was working on a study and discovered an "eat me" signal that counteracted the "don't eat me" signal.

They had observed how lots of normal cells used the "don't eat me" signal when going from one part of the bloodstream to another, and when the CD47 was up-regulated it shut back down in the tissue as a precaution. And when trying to solve this problem, Chao discovered the "eat me" that proved the key difference between cancer cells and healthy cells.

"Mark showed that he could have the insight, maybe through reading the literature or maybe just by looking at other fields, to say what could be the 'eat me' signals," Weissman said. "Now it's become a whole field." — *Max Gelman*

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- Name **Emily Drabant Conley**
- Company **Federation Bio**
- Position **CEO**
- Age **39**

**From genetics to the microbiome, Emily Drabant Conley 'captivated us all'**

One click of a mouse and Emily Drabant Conley may not have ended up at 23andMe.

The Stanford University grad student was about to delete an email about an upcoming career fair when she saw the name at the top of the list: 23andMe. At the time, the company was about 30 people large — "not well known, to say the least," Drabant Conley said.

But she had a mentor, who had a friend, who recommended looking into the startup. So she went to the fair, where she learned they needed someone to run neuroscience research. Drabant Conley found herself in a meeting with CEO Anne Wojcicki.

"It was instantaneous, the connection with her and with the company," Drabant Conley said.

Wojcicki felt the same.

"From the moment I interviewed Emily I knew she was capable of accomplishing great things," Wojcicki wrote in an email to Endpoints. "Emily walked in the door with brains, energy and confidence and captivated us all!"

Drabant Conley stayed with 23andMe for more than 10 years, watching it blossom into one of the

buzziest names in genetics and personalized medicine before leaving in July to take the helm at Federation Bio. When she left, the company had about 600 employees.

Now she's leading the charge behind a new type of microbiome company. Departing from her neuroscience roots and leaning on now years of biotech experience, she's hoping to turn naturally occurring bacteria against rare diseases like secondary hyperoxaluria (where the body absorbs an excess of oxalate, which is naturally found in food) and cancer.

Genetics piqued Drabant Conley's interest as a teenager during one of her earliest jobs teaching swim lessons to children with disabilities. She had just wanted to save up for a car, but quickly became interested in the science behind what makes us different.

She got her bachelor's in psychology and business from Vanderbilt University, then took a job as a research fellow at the NIH in 2003, which she describes as "Disneyland for scientists."

Drabant Conley was part of a research lab at the National Institute of Mental Health doing genetics research and functional brain imaging, "which at the time was really exciting and a very new technology," she said. She thrived on the big campus, with plenty of resources, smart scientists, and things to learn.

"I totally fell in love with science," Drabant Conley said.

When she later arrived at Stanford to pursue a PhD in neuroscience, her dream was to become an academic scientist with her own lab. But by the end of grad school, the vision had changed.

“I started to feel frustrated at the impact that I felt like I could have as a single scientist,” she said. “I felt like science is this huge, giant puzzle and I was working on one tiny corner of one tiny piece. And I wanted to be able to step back and be part of the puzzle in a more complete way.”

That’s when she met Carol Nast, who consulted at Genentech and soon became a mentor to Drabant Conley. It was one of Nast’s friends who recommended checking out 23andMe.

When Drabant Conley joined 23andMe, the staff was mostly scientists and engineers. They had just launched what they hoped would be the largest genetic study of Parkinson’s disease in the world, and Drabant Conley was brought in to run it. Then as more companies expressed interest in partnering with 23andMe, she shifted into business development.

It was a difficult role. The human genome project had come and gone and, with it, the promise that decoding DNA would bring quick cures. Drugmakers were skeptical 23andMe could help.

“There was kind of a hangover from that effort, where several years in it was like, ‘Well, we hadn’t solved all diseases yet, what a disappointment,’” she said.

But at 23andMe, the belief was that if you had genetic data on thousands or millions of people, you could conduct research as easily doing a Google search, using genes associated with disease to better identify new drug targets. By the end of her career at 23andMe, just about every pharma and biotech was trying to get greater access to genetic information to inform the way they discover and validate drug targets, Drabant Conley said.

One of her proudest accomplishments was putting together a $300 million collaboration deal with GlaxoSmithKline in 2018, a top project for GSK R&D chief Hal Barron, which she negotiated while in labor with her second child. With a laugh, she recalled muting her phone during a call with GSK while she was going through contractions.

“That felt like a privilege to me honestly, to be able to do that and to see that deal get done, kind of just in the nick of time,” she said.

Last year, a recruiter with Federation Bio reached out to Drabant Conley about the open CEO position. She was hesitant to take the call, but interested in speaking with co-founder and Venrock partner Racquel Bracken.

“Venture capital is a field that is mostly dominated by men, and so I am always keen to meet women VCs,” Drabant Conley said. “And then lo and behold, it was such a surprise to me that this ended up being my new career home.”

Drabant Conley said she was drawn to parallels she saw between the microbiome space and the

genetics space. She saw the potential to make an impact in a new field, where a bunch of microbial medicines have reached the clinic but have yet to get FDA approval.

“It’s totally fascinating — if you look at a human, we have about 20,000 genes. If you look at your microbiome, so all the bacteria that live in and on you, it’s about 20 million genes. So it’s orders of magnitude more complex,” Drabant Conley said.

Now the CEO’s main focus is getting Federation’s lead candidate, a “consortia of naturally occurring bacteria” to treat secondary hyperoxaluria, a rare kidney disease, into the clinic by the second half of 2022.

“There have been technical advances that are enabling us to study the microbes inside us in a scalable way,” she said. “And I think we’re just at the very beginning of our understanding of the microbiome and the many ways that it impacts human health.” — *Nicole DeFeudis*

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- Name **Leen Kawas**
- Company **Athira Pharma**
- Position **CEO, Founder**
- Age **35**

**Leen Kawas journeys from Amman to Washington in search of the world’s hardest cure**

From a young age, Leen Kawas knew she wanted to get into medicine.

Kawas lost her grandmother to cancer at age 7, and then lost her grandmother to Alzheimer's and her mother to another condition while still growing up in Amman, Jordan. What she found most troubling was that there were no treatments with any tangible benefits. So she set out to make one herself.

"I remember telling my dad I'm going to grow up and find cures for cancer," Kawas told Endpoints.

In the nearly three decades since, Kawas has poured her drive into science, helping launch the Alzheimer's-focused Athira Pharma. And while they're not focusing on cancer, the Seattle biotech is still attracting a lot of attention, as well as some big-name investors, in an area where many big companies have come up empty.

While in school, Kawas discovered a passion for chemistry. She said she was one of only four people in her year to ace Jordan's national chemistry exam — and also the only girl. But she struggled to envision how she could apply her knowledge to something tangible to achieve her ambitions.

The entrepreneurial spirit that's so prevalent in the United States is almost non-existent in her home country, Kawas said. Without realizing that she could take her research and launch it into a company, Kawas instead started a career as a pharmacist, only to find that path didn't quite suit her.

After only three months, she gave up the pharmacy life and went back to school for her PhD. Kawas settled on Washington State University, working in Joe Harding's neuroscience lab. She held a postdoc position for a little over a year before deciding that wouldn't be the right line of work for her, either.

What the postdoc did do, however, is instill in her that sense of entrepreneurship. Kawas began taking in as much as she could, learning "on the fly" both the nuts and bolts of industry, as well as how to network with insiders. Ultimately, Harding came to her with the idea to take one of their lab projects and launch it into a company.

"When he had this technology, he had other people, other candidates around him that he could have also approached," Kawas said. "But he came to me and he's like, 'You can do this.' And I didn't know exactly what he was talking about."

From there sprung Athira, with Kawas as CEO. And it wasn't a job she had to take, Kawas said, because she had another offer on the table from a different biotech. But when she told the other company about the opportunity with Harding, they discouraged her from taking the position they'd offered. That sealed the deal for Kawas' newfound excitement as an entrepreneur.

Throughout Athira's first year in 2011, the platform technology was still in very early stages, and Kawas spent most of her time networking to try to raise seed capital. Toward the end of that period, she managed to secure some cash not only from industry but also from Washington's public life sciences fund. Although it wasn't a substantial amount of money, it provided a key validation in allowing Athira to hire talent and lock down its business strategy.

After discovering their lead compound in 2015, Athira optimized it for use fairly quickly and had it in the clinic within two years. It's been full steam ahead since then, with the biotech going public last September and the compound, dubbed ATH-1017, currently in two Alzheimer's studies — a Phase II/III trial and an additional Phase II.

But Kawas and her team are highly cognizant of all that's come before them in this field. Amyloid beta and tau have forced even the biggest names in pharma to shake their heads in frustration, so what can Athira do to separate themselves from the pack?

Kawas says it's their focus on repairing neural pathways, by stimulating a receptor called HGF-MET, rather than removing the buildup of toxins in the brain.

"Of course there has been a lot of learning from these past attempts, we have to appreciate that those

past attempts definitely helped the field in general," Kawas said. "For us, we are agnostic to the pathology of the underlying disease. We are actually working on regeneration, which has a completely different profile."

They're going after mild to moderate cases in the early stages of Alzheimer's disease, but Kawas thinks the regenerative approach can eventually work for all patients. It's here where the program has thus far shown the most rapid improvement in restoring brain cell function, and FDA has been receptive to their technique given the candidate is safe and shows efficacy, Kawas said.

Could this be the future of Alzheimer's research? Kawas is hopeful but understandably reluctant to answer the question just yet. Rather than make any definitive declarations, she is just glad that Athira — a company she helped build from the ground up — has garnered excitement for its different approach.

"Especially with Covid now, we need to think outside the box," Kawas said. "With or without Covid, Alzheimer's is a national challenge." — *Max Gelman*

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- Name **Juliette Hordeaux**
- Company **University of Pennsylvania**
- Position **Senior Director, Translational Sciences**
- Age **37**

**Juliette Hordeaux, one of Jim Wilson's #2, finds herself at the heart of controversy**

Juliette Hordeaux was a year past her PhD, living in northern France, dissecting cats and dogs for a research firm, and bored out of her mind, when a message appeared one night on LinkedIn. It was a recruiter, who asked if she was familiar with Jim Wilson, the famous gene therapy pioneer. He said Wilson was looking for someone with her resume.

"I said, are you making this up?" Hordeaux recalls.

Hordeaux knew Wilson's work well. Before the research firm, she had studied under Phillipe Moullier, his former grad student, a position she fell into after finding the traditional spaying and neutering and vaccinating tasks of vet work too routine. She worked on treatments for pain and built her own experimental therapy for the deadly lysosomal disorder Pompe disease as she worked toward her PhD — always restless, always bouncing from one thing to the next. But then graduation came and, with the number of research jobs in France limited, she had to choose between her career and her country.

She chose her country, and it wasn't going well. Here was a once-in-a-lifetime chance to go back. So she hopped on a plane to Pennsylvania with her husband, a 3-year-old daughter, and another newborn on the way.

**"**I enjoyed everything I do for a while until I get bored, so I needed to be constantly challenged," Hordeaux says. "I think the only way to do that is to become a scientist and do research. I needed to come back each day not knowing what's going to happen."

It was a fortuitous time for Hordeaux to start a career in gene therapy, not only for her but also for the field. After more than a decade in the margins, research was now roaring back, driven by VC dollars and bolstered by safer technology developed in large part out of Wilson's lab. Early trials were already showing profound proof-of-concept data, and it seemed, Hordeaux recalls, as if the field would glide into the future, unencumbered by the safety concerns that devastated it a decade prior.

Hordeaux, depending on who you ask, would become part of the reason that it didn't, or part of the reason that it still might. Meticulous and tenacious, she would rely on the skills she developed dissecting cats and dogs and other animals to document dangerous side effects gene therapy could trigger in monkeys. It shook the field, winning acclaim and vitriol in equal measure. Then, she developed ways to fix them.

She was "super smart, almost fearless in her science," Wilson says. "She's constantly thinking about how to improve the technology."

The controversy started only months after she arrived in Pennsylvania, when Wilson assigned her to run a translational study for a rare disease therapy they had been developing. He told her it'd be in the clinic within two months. "It's an easy project," he said. "Then we'll move on to something else." But when they sent the monkey data to two toxicologists — a standard procedure — one of them noticed something: The monkeys' nerves were inflamed.

At first, Hordeaux and the lab thought it was an aberration. But when they ran the experiment again, the same inflammation came up. And again and again. In 2018, she and Wilson published their findings, documenting how the AAV9 virus — by that point, one of the most common ways of delivering genes into patients — could lead to toxic inflammation in a cluster of cells called DRG neurons.

It was a big deal, grabbing headlines in *Forbes* and the industry press. Wilson stepped down from the advisory board of the biotech Solid Bio, which was dosing patients with high amounts of AAV. But Hordeaux wasn't awash in praise.

"I was perhaps a bit naïve," she says. "I thought it was science, we're putting it out there because the field needs to progress. But then some people were pretty aggressive."

Reached by a reporter, AveXis's CMO put out a statement all but denying the study, attributing it to a problem with the way Wilson's lab made the vector. After another paper showing toxicities, Hordeaux said an executive from one company came up to her at a conference and demanded to know why she was putting out these results and accusing her of setting back the field.

Hordeaux held firm. Wilson told her she had discovered it, so now she had to fix it. Slowly, the side

project became her main focus. She pinned the inflammation on over-expression of the gene in DRG neurons and began researching ways of canceling the expression out.

She settled on a technique called microRNAs, a natural way for the body to regulate genes. Some microRNAs are only found in DRGs. If you incorporate them into the vector, the microRNAs in the cell bind to the ones in the DRGs, effectively neutralizing the therapy in those cells.

The results appeared in *Science Translational Medicine* last year. A handful of companies, she says, have now reached out about employing the technology in their work.

It's the kind of work, though, that you couldn't do in a company or even in most academic labs. Wilson's Gene Therapy Center allowed her to focus on translational work while also giving her the freedom to toy with important scientific questions, without having to worry about progressing a drug before they need to go back to investors.

Still, most of her work does go into direct translation. Having shot up the ranks, Hordeaux is now a director, leading both the Gene Therpay Center's 13-person histophathology team and a research team of 10 people who are developing 12 different therapies, including a different version of the one she built in grad school: a possible cure for Pompe disease. She likes the director gig, she says. She misses the bench sometimes but can now work on numerous different projects at once.

"I really like that I can move now fast that I have a team," she says. "I'm kind of impatient."

It's a role that Wilson says she's excelled in.

"What I didn't know was how good a manager she'd be," Wilson says. "She's turned out to be a phenomenal manager."

That impatience, though, can't get in the way of the nitty-gritty work. She thinks the field is starting to adopt that view, too, as more companies recognize the need to first study these therapies in monkeys.

"I think everything that has been publicly available, every safety signal that has shown up in clinical trials, if you look back, there was always some indication this could happen from the non-human primate studies," she said. "If you want a clean tox study, you do it in mice." — *Jason Mast*

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- Name **Eric Kelsic**
- Company **Dyno**
- Position **CEO, Founder**
- Age **37**

**Eric Kelsic tries to start a gene therapy revolution**

Growing up in Colorado, Eric Kelsic was the kind of kid who asked questions: Why did magnets repel or attract? How did electricity work? What was the structure of the atom? A steady storm of curiosity, of interrogations ad infinitum, that his teachers could never quite satisfy.

He went off to CalTech, where kids with too many questions go, and studied physics. He learned that his answers lay in math, that, at the bottom, the universe was abstraction, a complex web of equations and relations that existed nowhere and held up everything. He was satisfied. And restless. The work was *too* abstract, detached from any clear application. He wanted to solve problems.

So, with his undergraduate months expiring, he convinced a bio-engineer, Christina Smolke, to let him work in her lab over the summer. By then, he found biology held science's biggest remaining mysteries and that modern biology was math too — not the memorization he had done in high school. Having missed by months the deadline to apply for an official position, he volunteered to work for free; Smolke helped him find outside funding to stock shelves, clean beakers and monitor cell cultures while he designed his own experiment around genetic circuits.

"It was a really interesting job, part-technician, part-time lab manager," he says. "It was one of those lucky breaks."

It was a humble beginning for a man who, in the last two years, has become a quiet celebrity around the drug-making world, signing billion-dollar deals with its biggest players: Roche, Novartis, Sarepta. In 2018, more than a decade after his brief opening tour at a bioengineering lab, Kelsic would take the stage at an academic conference and, in a rare and gaudy move, walk the field through their unpublished work on a project meant to revolutionize gene therapy.

His phone started ringing immediately after, with calls from investors and executives who were as impressed by his work and vision as they were floored by his willingness to disclose it in such detail before he had even started a company.

“That was not something you would typically do in an extremely competitive field and more than a year before publication. We just told everyone what we were doing at the biggest conference in gene therapy,” Kelsic said. “But we also felt like we were far enough ahead.”

Kelsic wanted to re-engineer the molecular shuttles that researchers use to deliver genes into human cells: a class of (largely) harmless viruses called adeno-associated viruses, or AAVs. Far safer than the vectors researchers first used in the 90s, these viruses helped bring back gene therapy from the margins. But the industry was quickly pushing the technology’s limits: Existing AAVs didn’t necessarily deliver the gene to the right tissues, they were difficult to manufacture, they led to safety issues when developers upped the dosage and not all patients could receive it.

To solve the issue, Kelsic and a small team at Harvard’s Church lab set up a vast DNA library containing AAV sequences, tweaked each just a little and shot them through tests in mice or monkeys, measuring how they performed on various metrics and which organs they reached. With each iteration,

a machine learning platform learned which mutations are most beneficial and harmful, beginning to allow researchers to design new ones that have the ideal combination of traits.

AAVs are delicate combinations of proteins, weaved together like lattice. Shifting just one amino acid can make them fall apart, as a generation of frustrated bioengineers discovered. Kelsic and his company, Dyno, wanted to make them fully tunable for the first time.

“This was by far the best application that I’d ever seen of AI in biology,” Alan Crane, Dyno’s chairperson and an investor at Polaris, who invested after he attended the conference, told Endpoints last year.

Kelsic got the idea after he wrapped up his PhD at Harvard, where he had become an expert in protein engineering. He wanted to go into industry next. That’s where people really solved problems, he thought. He didn’t have much experience in biotech, but he knew George Church, the heavily connected geneticist, from his dissertation committee. He figured he could spend a few months at the Church lab, completing a project that would prove to companies he was an asset.

He would spend nearly 4 years there. Church pointed him to the AAV problem and, under the guise of Vicki Sato’s famed “commercializing science” course, he confirmed with investors and executives that this was genuinely a problem — that if he solved it, he could make an impact.

That was the easy part. Building it was harder. Kelsic was convinced new tools for rapid DNA synthesis and DNA sequencing could make it far easier to engineer proteins. Turning those tools into a system, though, was easier said than done. Pierce Ogden, the graduate student who worked with Kelsic, said their first two years of efforts failed, until one late night in the lab, as they looked over another blown experiment, Kelsic looked up and said, “What if we do it like this?”

“There wasn’t much time to worry about whether it would work or not,” Ogden says. “In a matter of weeks, we were just generating insane amounts of data.”

He could be like that, thoughtful yet instantaneously decisive. He has a habit of pausing at length after questions or mid-conversation before offering long and detailed answers. He doesn’t give up easily, Ogden says.

The result is that Kelsic is now able to talk humbly yet confidently about changing millions of lives. Most biotechs develop their own drugs. Kelsic has focused Dyno and their rapidly growing staff on solving the AAV problem and then licensing the vehicle to other companies for use in can use their products, multiplying their impact across diseases and drugs.

If he manages to pull it off, the gene therapy field could not only cure some of the rare diseases that current AAVs have struggled to hit, such as Duchenne muscular dystrophy and cystic fibrosis, but also

larger diseases. You could even add new genes as opposed to just fixing broken ones.

Some of those will come soon, he offers calmly. Within 3 to 5 years, their AAVs should be 100 to 1000 times more efficient.

“It’s such an exciting and elegant way to treat disease, and it enables us to do so many things that are unattainable today,” Kelsic said. If they can improve the vehicles, “you could think about using it for treating disease, preventing disease, or even helping people live easier, healthier lives.” — *Jason Mast*

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- Name **Mike Klichinsky**
- Company **Carisma**
- Position **Founder, VP of Research**
- Age **31**

**The quiet wunderkind behind the next potential wave of cancer-melting CARs**

Mike Klichinsky considers his work ethic a family trait.

His parents, immigrants from the Soviet Union, came to the US in 1990 with a mission to better themselves and succeed in their respective fields. Klichinsky took that education to heart.

It’s rare that someone in their early 30s can call themselves a potentially revolutionary inventor, but that descriptor has settled on Klichinsky’s able shoulders. Crafting the technology behind CAR-M at Carl June’s famed cell immunotherapy center at Penn, Klichinsky is now the VP of discovery science at

Carisma Therapeutics, the biotech he started up alongside his erstwhile professor and current collaborator Saar Gill. Earlier this month, the company dosed its first patient with a CAR-M candidate for solid tumors, potentially setting the stage for a new generation of immunotherapies.

When Klichinsky wrapped up high school at the tender age of 16 and started pharmacy school in 2007 at the University of the Sciences in Philadelphia, all that success may have felt a long way away. A Philly native, Klichinsky followed the example of his mother, a Temple University graduate who is also a pharmacist by trade, and took a liking to the technical side of his program— so much so that his expansive curiosity eventually hit its boundaries.

“It was fantastic,” he said. “You learn everything you need to know about drugs, even things you wouldn’t think about, like how to pack a capsule or turn a powder into a tablet. Quite early on, I realized I really like the research part of this — I had all these questions, and in the context of a pharmacy program you can’t get all those questions answered.”

But the school did afford Klichinsky an opportunity to dive into research on a limited scale — some rat studies looking at the effect of the antimalarial hydroxychloroquine on cancer cells, for instance. In 2010, he took a role at the Wistar Institute at Penn working with Paul Lieberman. His team focused on the epigenetics of the Epstein-Barr virus: how the virus conceals itself and can lead to cancer.

That experience helped push Klichinsky to pursue a doctorate at Penn for pharmacology and into two professional relationships that have come to define his career. While on clinical rounds at the university, Klichinsky was randomly assigned to the leukemia ward, where attending was another young doctor: Gill. When Gill founded his own lab, Klichinsky was the first student to join up. Alongside the eminent Carl June, Gill would co-mentor Klichinsky’s eventual thesis exploring the use of engineered macrophages.

But the work didn’t start that way. At first, Gill’s lab chased a CAR-T therapy for Epstein-Barr, which Klichinsky described as “interesting,” if ultimately a loser.

“It was working, but there were some technical challenges,” he said. “We made the decision that this is a project where it’s just another CAR against another target. One of the best decisions we ever made was to kill that project.”

What began as an interest in macrophages, one of the most abundant immune cells in the tumor microenvironment, soon turned into an area ripe for innovation. With June and Gill’s backing, Klichinsky chased the idea that unlike T cells and NK cells, macrophages don’t just kill cells but also “eat” them, and therefore could be redirected to consume a broad range of targets. Klichinsky was hesitant, at first, to pursue the idea given June’s pioneering work in CAR-Ts, but he found a willing backer.

“(June) said, and I’ll always remember this, you know we don’t have a T cell system, we have an immune system, and these cells all work together — so go for it,’” Klichinsky said.

The initial CAR-M was directed at CD19, no surprise given Penn’s pioneering work on that target. After that initial experiment worked, Klichinsky and the team aimed CAR-Ms at HER2-expressing solid tumors — what is now the lead program at Carisma. With a novel technology on their hands and the possibility of offering a parallel approach to CAR-T therapies, it didn’t take long for Klichinsky and Gill to realize they had a business on their hands. Enter Carma Therapeutics, which the co-founders eventually changed to Carisma after potential trademarking issue came to light.

The first couple years of Carisma’s growth went slowly as Klichinsky finished his doctorate — a wise move in its own right to invest in his future. The fledgling biotech was guided by June, who took a seat on the scientific advisory board, as well as Bruce Peacock, an investor and serial entrepreneur out of

Pennsylvania who helped jumpstart the company's development.

Before Klichinsky made the full-time move to Carisma in 2018, the team brought on Steve Kelly, a pharma executive with more than 30 years of experience in the space, most recently as CEO of the oncology biotech Pinteon Therapeutics.

Kelly was familiar with Klichinsky's work after seeing his thesis presented at AACR and was looking for an opportunity to jump back into the early oncology space. After cold calling Gill to ask about a position, Kelly was hired on as CEO in February 2018. He consulted with Klichinsky about a position on the team, eventually offering him a role as head of discovery. In one of his first meetings, Kelly asked Klichinsky to come up with a game plan for what he wanted to do with the company's CAR-M platform.

"A week later, he came back to me with literally a 70-page Excel spreadsheet and said, 'OK, this is what we need to do,'" Kelly said. "It was that breadth of enthusiasm and ideas. It was great to have him come in with that."

Taking a discovery role at a company developing the technology you created isn't always intuitive for founders. But according to Kelly, Klichinsky is far more interested in seeing how far he can take his platform than what title he can secure for himself.

"He has no ego," Kelly said. "I've worked with a number of founders who have the ego to go along with their brains. (Klichinsky) is modest, and he's very collaborative and deferential. He's working with people who have been working in research for longer than he's been alive, in some cases. But he understands that."

Another seasoned pharma vet sees that same collaborative spirit from Klichinsky. CMO Debora Barton joined the team in November 2019 after stints at Novartis and Celgene. Taking the leap to what she called "by far the smallest" company she's ever worked for wasn't a shoo-in decision, but Barton said the promise of Klichinsky's technology — as well as his commitment to success — has eased the transition for her.

"He's very bright, he's very collaborative, very open minded," she said. "It's honestly a pleasure to work with him."

That sense of collaboration and being open to mentorship is part of what has guided Klichinsky's work and ability to innovate, he said. That means being humble and acknowledging what you do and don't know.

"I guess my advice is to identify the right mentors," he said. "It sounds easier than it is, and there's an element of luck, but I owe my success to hard work and being very fortunate with the people I was

exposed to.” — *Kyle Blankenship*

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- Name **Nicole Gaudelli**
- Company **Beam Therapeutics**
- Position **Head of Gene Editing Technologies**
- Age **36**

- Name **Alexis Komor**
- Company **UC-San Diego**
- Position **Assistant Professor**
- Age **34**

**An 'unstoppable' duo weaves contrasting threads together to engineer CRISPR 2.0**

When Alexis Komor joined David Liu's famed Harvard lab, Nicole Gaudelli was the first person she was introduced to.

Other than being the only women in the group and applying for the same postdoc fellowship, the two had little in common. In fact, Komor recalled her confusion receiving edited proposals from Liu about phage-assisted continuous evolution of antibiotics — the project Gaudelli had been working on — when she was discussing DNA editing with him over email. Outside of work (they didn't even go to the same subgroup meetings), Komor was the California-bred, matter-of-fact inorganic chemist to Gaudelli's effervescent organic chemist with an East Coast flavor.

It turned out to be the perfect recipe for pioneering a new way to edit the genome. Together, they invented the base editors that undergird Beam Therapeutics, the high-flying biotech the duo helped create with Liu, Feng Zhang and J. Keith Joung, all luminaries in the CRISPR field.

"Well," Komor told Endpoints in an interview, "we say it was just meant to be."

For Gaudelli, the love of science has always been personal. Just as expeditions with her grandfather involving fish, rocks, flowers and sometimes raccoons fostered a connection to the natural world, experiments she would do with her father at home — from rock tumbling to DIY nylon — and with her

chemistry teachers in school (blowing methane into soap bubbles then igniting them, to take a wild example) made science visibly exciting.

It wasn't until she took a research job with Steve Bruner as an undergrad at Boston College that she started looking into molecular biology as a way to improve human medicines. There, she realized the urgency of the antibacterial resistance crisis and the dramatic need for discovering or engineering new classes of antibiotics. The transition was gradual, but it ran deep.

"A lot of things that anybody's interested in, you really love them or are interested in because your mentors are, and you have a relationship with your mentor, and their enthusiasm sort of bleeds over to you," Gaudelli said.

After spending seven PhD years at Johns Hopkins elucidating how monobactams are made in nature — in an effort to single out the intermediates and substrates and enzymes that scientists would need to manipulate if they want to synthesize better antibiotics — she wanted to explore that next step: prodding those antibiotics to do something unnatural in a way that makes them better drugs.

So she headed to the Liu lab, where she met Komor, who likes to warn listeners that the story about how she got into chemistry was a boring one. In retrospect, she wouldn't recommend others making the decisions that she did based on her reasoning: studying chemistry because that's the only science degree at UC-Berkeley that confers a BS and not a BA; staying in the inorganic chemistry field for her PhD just because she had been in it. But at those stages, they all made sense.

As she found a fondness for nucleic acid chemistry and Liu pushed her to look at the DNA binding protein Cas9, though, she quickly spotted something that didn't.

Having trained at CalTech with Jackie Barton, who specialized in DNA damage and repair, Komor was perplexed by the widely accepted idea of using double-stranded breaks to do gene editing — which, as any DNA damage person would tell you, is "the worst type of DNA damage ever."

There must be a way to modify the nucleotides of DNA in a less toxic way, she reckoned.

"It was a very naive chemical biologist delving into the genome editing field, which is how base editing came around," she said. "It's just like a new perspective on the field from someone who didn't know any better."

Coming into a totally new field, Komor also had no experience with basic techniques like cloning or purifying protein. Gaudelli showed her how — while she was still left sorting out the best combination between an infinite number of possibilities for putting together a base editor: with the right deaminase that would chemically convert a letter into another, and the right linker that attaches it to the right spot on Cas9. Then there was the gel assay she designed to find out whether it's working — which took up 70% of her time but ended up being one subpart of one figure of the manuscript describing a C to T editor.

"Every time I did it, helped her with an experiment, I was like, oh this looks like it works," Gaudelli recalled. "See, here's the protein, you run the gel, looks like there was a band shift. Well OK, then we go and do the next thing and then I found myself sort of staying up at night thinking more and more about DNA and DNA manipulation and protein and small molecules."

Gaudelli soon faced a tough choice. Now that Komor had laid the foundation for what a base editor can

be, utilizing naturally occurring enzymes, it opened up a yawning gap for new tools that would make other types of changes, say converting an A to a G — thereby addressing a much wider spectrum of diseases. An enzyme that could do it, though, doesn't exist in nature. She realized that her experience in directed evolution and protein engineering could come into use. So she began working on it in background, until there came a time when she had to drop something. She chose to leave the decade of antibiotics work behind.

"I always say I'm a distracted natural product chemist living in a genome editing world," Gaudelli, one of the first employees at Beam and now its head of gene editing technologies. "I still sort of see myself as a chemistry person and somehow I got tangled up in all this."

She still has a pipe dream of applying gene editing to antibiotics, but for now, Komor is the one carrying on the academic work. Her lab at UCSD has three subgroups: one deploying base editors to study functional genomics in a way that genome-wide association studies can't; another to develop new editing tools; and a third trying to understand how the tools actually work.

When it comes to envisioning biomedical research of the future, their answers echo the same theme of openness. Komor talks about the need for formal training for academics in culturally sensitive teaching and mentoring styles so that everybody has the same chance to succeed, while Gaudelli wants to lead by example in fostering transparency, depositing sequences of her editors so others can learn.

"This time we're in is bigger than any one person," Gaudelli said. "And the more we share and collaborate, whether you work at Beam or not, the more benefit we'll get, the more we'll learn from each other, the faster we'll be able to get to the right answer."

Now separated by the whole continent, the two are still united by their passion and dedication to a field they helped create, Liu said.

“Nicole wears her feelings on her sleeve and so much of what she does is shaped by her empathy, while Alexis tackles life’s challenges with more of an analytical approach, often stopping to reflect on life’s ironies along the way with her dry sense of humor,” he observed. “Together they are unstoppable.” — *Amber Tong*

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- Name **Marc Lajoie**
- Company **Outpace Bio**
- Position **CEO, Founder**
- Age **35**

- Name **Scott Boyken**
- Company **Outpace Bio**
- Position **CSO, Founder**
- Age **35**

**Marc Lajoie and Scott Boyken reimagine the possibility of proteins**

Like many 18-year-olds starting college, Scott Boyken had no idea what he wanted to do with his life.

He began his undergrad career as a music student and changed his mind several times before settling on a computer science and biology double major. Consumed by the drive to create new things, Boyken found his way to the Iowa State doctoral program for computational biology.

“I’d always wanted to find something where I could combine understanding how things work with creating new things,” Boyken says. At Iowa State, “I really fell in love with proteins and studying structural biology ... by the end of that, I knew I really wanted to do protein design.”

While studying there, he met Marc Lajoie, a young researcher who was working with George Church on new genetic technologies, at a conference in Germany in 2011, and the two became fast friends. Ultimately, Boyken and Lajoie teamed up at David Baker’s protein engineering lab at the University of Washington, where they would help provide the foundation for Rick Klausner’s star-studded Lyell and then spin out their own company in Outpace Bio.

The professional relationship between the two started early in their postdoctoral work at Washington, and they heaped praise on one another throughout their discussion with Endpoints. Lajoie would often approach Boyken, who he described as one of the best protein designers, if not the best, in the program.

Their big breakthrough was a project involving de novo protein design that Lajoie calls “locker switches,” which he says are essentially proteins with no prescribed biological function. Whereas proteins that have evolved naturally over billions of years have done so to accomplish specific functions, the proteins Boyken and Lajoie are designing can be fine-tuned to do whatever they want.

Lajoie compared the approach to making customized parts for modern electronics. In order to make a smartphone, one needs to refine raw materials rather than picking things off the ground or in trees.

“It’s the same thing with these de novo proteins. You can go and re-use stuff that’s out there, and there’s a tremendous amount of biology that’s out there,” Lajoie said. “But in the end, when you want to program a really specific function, you need custom-designed parts.”

Those locker switch projects from the Baker Lab, with their relatively easy programmability, eventually caught Klausner’s attention at Lyell. Klausner explained how the tech could be applied to the next generation of cell therapies, and they got started at the company in early 2019.

It was a far cry from where Lajoie thought he’d be. While Boyken was jumping around majors as an undergrad, Lajoie was fairly certain he wanted to work in something with science. He geeked out over organic chemistry and drug design, but early on he “didn’t really know biotech was a thing,” he said.

Boyken and Lajoie spent their time working with the all-star team at Lyell, and got to the point where the company was ready to test a number of their hypotheses. Lajoie said the nearly two years they spent there was a “really productive” research period, and in order to get everything into the clinic and work on their own collaborations, Klausner suggested last summer they spin out into their own

biotech.

Thus, Outpace Bio was born, where Lajoie serves as CEO and Boyken as CSO. There isn't much the duo is ready to talk about yet, and the biotech's website is barren. But they recently unveiled a $30 million round and a solid tumor partnership with Lyell. Lajoie added that their focus on the locker switches will encompass a broader scope than their projects at Lyell.

As the fields of cell and gene therapy move forward, Outpace is taking stock of where the science is right now in order to map out the future. There are currently three FDA-approved T cell therapies, Lajoie said, but they all target CD19 and still don't have efficacy in solid tumors. Lajoie and Boyken believe the cells involved are making the wrong decisions, even though they're doing as they learned during eons of natural evolution.

Where they hope Outpace can step in is to reprogram that biology to fight disease.

"We see our role in cell therapy as creating a way to break cells free from their evolutionarily pre-programmed decision-making processes," Lajoie said. "The diseases that the industry has been banging its head against for decades, without being able to find a cure — the fundamental reason behind that is that these diseases are too complex for a single molecule to overcome."

But all they helped contribute to these two buzzy biotechs very nearly never happened — in the summer of 2018, about a year before Lyell emerged from stealth, Boyken and Lajoie were in the middle of preparing their faculty proposals. The pair who ended up leading Lyell's protein and cell engineering were a smidge away from becoming college professors before Klausner reached out.

"Long story short, Rick is a great salesman," Lajoie said. — *Max Gelman*

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- Name **Joshua Liang**
- Company **Clover Biopharmaceuticals**
- Position **CEO**
- Age **29**

**The humble son steering China and CEPI's dark-horse Covid-19 vaccine**

CEPI's Covid-19 portfolio features several recognizable names. The vaccine developer was given the largest grant by the Oslo-based group — ranking just below Novavax and the Oxford/AstraZeneca team in total funding amount, debt or loan included — isn't one of them.

Clover Biopharmaceuticals' inclusion was notable for reasons other than the dollar figure. Based in Chengdu, Sichuan, it was the first (and only) Chinese biotech company to gain backing from the prestigious coalition that had been betting on a range of different technologies for epidemic preparedness. Its program was also the only one utilizing a covalently trimerized fusion protein as the vaccine antigen.

If you were expecting a rich backstory with frantic calls between scientists, though, prepare to be disappointed.

"So we had no previous knowledge of CEPI, we didn't know anyone at CEPI," CEO Joshua Liang said. "We just saw their call for proposals I think at the end of January, or maybe it was early February of last year, just on their website, and just applied."

By his telling, it just so happened that Clover's platform tech — invented by his father, who helped found the company — was well suited for viruses with a trimeric spike protein. They had also just

completed a commercial scale facility in Changxing, which has the capacity to produce hundreds of millions, if not a billion, doses annually. Seeing the spread in China at the beginning of 2020, "you immediately knew it is a program we need to initiate," Liang said, and once they were given the nod with CEPI, the coordination followed naturally, leading to adjuvant partnerships with GlaxoSmithKline and Dynavax. The vaccine candidate is now in Phase II/III.

But Xiangdong Wang, a co-founder of Clover and longtime family friend who may be better known for his part in starting BeiGene, would give him more credit than that.

"This is definitely not a small task," he said. "And they don't have a lot of help, in a way, like Moderna or Novavax got from the US or from the international organizations. Clover — they mainly just get help from CEPI. And that is all Joshua."

In a way, that one-of-its-kind position Clover occupies is illustrative of Liang, who had arrived in Chengdu from San Francisco just five years ago, barely conversational in Chinese.

He had grown up in Nashville — or as he would say, the labs of his father Peng Liang, who was a tenured professor at Vanderbilt — and got exposed to basic biology research early, digging up four o'clock flowers from his backyard and extracting the RNA to game out where the vivid colors came from.

It wasn't until his mother was diagnosed with breast cancer, just as he was working on the cancer protein TRAIL, that he set his eyes on a career in biotech. After completing a dual life sciences and management degree at the University of Pennsylvania and going through a slate of banking internships (plus one working on gene expression in Vertex), he decided he'd rather first learn, on a broader level, how the industry operates, taking a job at Centerview Partners.

It was a boom time for biopharma, and from his brief stint, he would take away lessons that became guideposts in his current job. Chief among them: Time is more valuable than money, science never lies, and to build a biotech company, you really need development capabilities, experienced operations and the ability to raise capital on top of strong science.

The largest deal he was involved in by far was AbbVie's $21 billion acquisition of Pharmacyclics, which ultimately gave it the blockbuster BTK inhibitor ibrutinib. It sparked a particularly fruitful conversation with Wang when they met over dim sum outside the JP Morgan conference in 2016, where Wang was doing roadshows for BeiGene — whose lead candidate also targeted BTK.

They chatted about Clover, and how the company, even with Peng Liang at the scientific helm, really needed someone to steer the business side. Wang, who sat on Clover's board, admitted he wasn't expecting much: It was a big ask for a second-generation American to make the move to his father's homeland.

“At that time we had about a dozen people in the company, all scientists at the research lab,” Liang said, switching naturally into first-person even though he didn’t work there then. “Everything was still in the preclinical or discovery phase. And I think we had about $1 million in the bank total. And the total in that 10 years I think they had only raised $10 million, something like that. So we had a big challenge.”

He was in. Three months after that lunch, he jumped on a flight to become Clover’s chief strategy officer.

After that, Wang said, “Clover simply took off.”

In a series of financing rounds over the next few years, the biotech raised more than $500 million to build out its pipeline of vaccines and cancer drugs. Seeing a lack of CDMOs that could reliably produce their biologics, Liang kickstarted a three-year construction of Clover’s own manufacturing facility, which was the first financing deal that he wrangled — with the local government. It now has a subsidiary in Australia, where it ran the initial trials for its Covid-19 vaccine candidate, among other places. And just in the past year, the headcount went from 175 to 500 — a result of sorting out what units needed to be built out, when and where to recruit.

Approaching his first anniversary as CEO, Liang draws inspiration from Roy Vagelos, the former Merck CEO who had set up the dual program he enrolled in at Penn.

“When Merck discovered a drug for river blindness and really the use in Africa wasn’t going to be a lucrative opportunity for Merck,” he said. “And then he just single-handedly made the decision to offer

it for free for the benefit of public health. Maybe short term, it wasn't lucrative for Merck. But longer term it ended up being great for Merck in terms of perception of public health and being able to attract the best talent."

Clover is no Merck — far from it. But if Liang gets his way and the Covid-19 vaccine candidate he helped invent reads out positive in the middle of this year as planned, it will be an enthusiastic partner in global collaborations and one of the first Chinese players in history to be exporting world-class vaccines. — *Amber Tong*

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- Name **Sean McClain**
- Company **AbSci**
- Position **CEO, Founder**
- Age **31**

**Sean McClain aims to simplify protein production**

Sean McClain graduated from college a year early and with an idea, one good enough to convince his then-fiancée to move in with his parents and spend her paycheck on a small basement lab in downtown Portland, OR.

It was 2011, and McClain was about 22 years old. He became obsessed with synthetic biology while studying biochemistry and molecular biology at the University of Arizona. He pointed to Genentech's insulin, which was first produced in E. coli, as inspiration behind his big idea.

Insulin was Genentech's big breakthrough, the first recombinant protein ever made in the lab. Then when the industry shifted to monoclonal antibodies, a more complex product, Genentech tried to produce them in E. coli — but E. coli just didn't have the machinery to do it. Genentech ended up using CHO or mammalian cells, which drove up time and cost, McClain said.

"I knew that if we could design E. coli to be more mammalian-like, it'd be a huge game-changer," he said.

So he and his then-fiancée (now wife) rented a 200-square-foot space in the garage level of a business incubator, which was essentially a broom closet turned low-tech lab. It was like a dungeon, he said. There were brand new labs on the top floor, but none were available at the time — and even if they were, McClain couldn't have afforded it.

He bought used lab equipment from surplus auction houses, some of them 80s-era rejects thrown out by big companies like Pfizer and Merck. (He recalls snagging a PCR machine, likely one of the first ones ever released, for 50 bucks.) He lugged the dingy pieces in with his slightly skeptical but helpful father.

"I could just see it on his face, he's like: 'You really want to do this?'" McClain said. He shrugged it off, thinking: "We can accomplish the world, and we're going to do it here in this basement lab."

Little by little, McClain built AbSci from the ground up, working on a more efficient way to manufacture proteins in E. coli. He eventually raised nearly $240 million in VC funds and landed partnerships with Sanofi and Merck.

“And it was just a ton of fun,” he said, smiling.

McClain spent the first 18 months developing the proof of concept for AbSci’s technology on a “shoestring budget,” while his fiancée, who worked in the incubator upstairs, crashed on a cot. They shared one car, and would make the 40-minute commute home late at night.

About two years in, McClain got $300,000 in angel funding, and six months later hired his first employee. They moved into a bioscience incubator in Portland, and the company took off. They’ve gone from 40 employees at the beginning of 2020 to 100 currently, and they’re on track to be at 225 by the end of the year.

“I’ve always known he’s had a really high level of drive,” McClain’s father, Rick, told Endpoints.

He recalled McClain’s first wrestling tournament as a kid. He wasn’t very good, his father admitted, but he wouldn’t leave until he won a match.

“He wrestled like seven matches before he finally got his win,” Rick McClain said, adding that he continued the sport all through high school. “He’s been a driven, passionate kid for all his entire life, and he’s just kind of had that entrepreneurial business spirit to go.”

AbSci went commercial in 2018 with its E. coli expression platform, SoluPro, for producing soluble, complex proteins in high yields. The following year, it introduced its protein printing platform, which builds on SoluPro with technology designed to pump out high-diversity strain libraries and high-throughput screening assays. That platform originated from a highly engineered E. coli strain built in the basement lab.

“We’re making protein production as simple as DNA synthesis,” McClain said.

The company pulled in a $65 million Series E round in October, which McClain tagged for expanding production capacity, including a new 60,000-square-foot facility in Vancouver.

“Many drugs, especially biological drugs, don’t make it to market or take forever to get to market, not because of drug discovery but manufacturability,” McClain told Endpoints at the time. “And what AbSci is doing is flipping that paradigm and allowing researchers to be able to focus on drug discovery.”

In January, McClain bought out Denovium and its AI engine, with the goal of unifying drug and cell line development. AbSci will feed the engine billions of data points on protein functionality and manufacturability that they’ve collected from every molecule and target they’ve worked on. The idea is that if they mine that data, they’ll be able to do full in-silico drug design and cell line development at the click of a button.

“Think of this as like the Google index search for drug discovery and cell line development,” he said.

While he’s proud of where he landed, McClain says some of his fondest memories are of the days and nights spent dreaming up AbSci in his “dungeon” lab.

“It’s just fun to see all the hard work pay off,” he said, “and really seeing that exciting adoption, seeing the vision through, and really truly the ability to change the world one protein at a time.” — *Nicole DeFeudis*

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- Name **Ben Oakes**
- Company **Scribe**
- Position **Founder, CEO**
- Age **32**

**Ben Oakes’ dive inside the human mind colors his leadership role at gene editing startup Scribe Therapeutics**

As an undergrad, Ben Oakes wanted to learn how the mind worked — so he chose to major in philosophy and neurobiology, a try-it-all approach that would eventually suit him well in the lab.

It was a double shot on goal that Oakes, a New Jersey native with big ideas about the nature of consciousness, thought would help answer some of his own big questions and give him the sense of purpose he craved. But the philosophical path — and a disheartening stint shadowing at an opioid-riddled rural ER during his undergrad — didn’t hit the right nerve for Oakes, who longed to get his

hands dirty in his pursuit of making a difference in medicine.

He got that chance at a small lab at Princeton in 2011 doing the messy work of engineering an open-source database for zinc finger nucleases for gene editing, a laborious process that served as Oakes' road to Damascus.

"It was the most transformative thing I've ever done," Oakes tells me. "It was incredibly difficult — I had gone from a very high level philosophy major thinking about how to think about the mind to an in-the-weeds molecular biologist."

What Oakes thought was cutting edge in gene editing, however, was about to change. In 2012 and 2013, Jennifer Doudna, Feng Zhang and Emmanuel Charpentier's work on CRISPR gene editing hit the science world like a nuclear bomb. Even as a relative novice, Oakes knew everything was about to change.

"I saw the writing on the wall right away," he said. "The second I saw Jennifer's paper, I was like, 'Holy shit, this is what I want to go do.'"

Ten years after finding his calling at the Lewis-Sigler Institute for Integrative Genomics, Oakes is now the CEO of gene editing startup Scribe Therapeutics, a company developing its own CRISPR platform around the CasX DNA snipping enzyme derived from groundwater bacteria.

Oakes' remarkable rise to the top is a story about precocious technical skill but also the desire to know everything about everything. After Princeton, Oakes scored a postdoc spot at Doudna's lab at UC-Berkeley in August 2013, but he wasn't immediately sure how his engineering background was going to fit onto the team with Doudna, a specialist in biochemistry.

"I'm a synthetic biologist with the engineering background; that is not the lab I fit in by any means," Oakes said. "I came in knowing that I was going to have to chart my own path between her lab and someone else's that was more interested in doing the sort of synthetic building that I wanted to do."

That's where Dave Savage came in. Savage would later go on to cofound Scribe alongside Oakes, Doudna and Brett Staahl, then a postdoc fellow in Doudna's lab. Savage's lab at UC-Berkeley focused both on the ways in which microorganisms make inorganic carbon organic and biosensors, and Oakes found a natural fit investigating a new path forward for protein engineering.

Over his four years straddling both labs, Oakes looked for new ways to engineer the Cas9 enzyme. But that "esoteric" work, as he described it, didn't hit the real-world application that Oakes craved. He started thinking about CRISPR's therapeutic potential from a new angle.

"What I realized was we would have to take a step back and go back to that pragmatic question and ask, 'What actually matters today in the world?'" he said. "My goal has always been therapeutics, still is therapeutics, and it became this question of what does a therapeutic application of CRISPR actually look like and what do we need to build to make it work?"

Those initial conversations with Doudna, Savage and Staahl planted the seeds for what eventually became Scribe. But making the leap to industry meant focusing on delivery, efficacy and specificity all while "not stepping on other people's toes" in terms of IP, Oakes said.

Enter CasX. After graduating in 2017, Oakes took a one-year fellowship at the Innovative Genomics Institute Doudna founded at Cal, exporting a team of existing peers to scan multiple protein enzymes for therapeutic use. Leaning on the university's resources, his team did much of the groundwork to establish CasX's potential in neurodegeneration, eventually scoring an initial $20 million funding round for Scribe in late 2018. The company recently followed that up with a $100 million round in March.

One of the key collaborators in getting Scribe off the ground was Staahl, a postdoc peer in Doudna's lab who in person appears the personality opposite of Oakes. Where Oakes is expansive and quick with a joke, Staahl is gruff and more guarded. But the partnership worked wonders.

Early in their work together, Staahl remembers an early readout of a Cas9 experiment in two different cell types — one of which showed clear efficacy and the other that was a bit murkier. Huddled over a computer late at night, Staahl showed Oakes the results.

"Ben's comment was 'that's great, that's awesome — now you just need to get it working on (the other one),'" Staahl tells me. "That's kind of how he is; he's always improving, he's always working toward a more perfect solution, and he acknowledges that we haven't explored anything fully yet."

As the team has grown over the past four years, it's scoured millions of protein variants to develop the technology that Biogen paid $15 million upfront and $400 million in milestones to partner on in October.

Along the way, Scribe picked up CBO Svetlana Lucas, an Amgen veteran with 20 years of experience in oncology, who was looking to start something new. When she took the interview with Scribe, she was skeptical of Oakes as CEO given his age. After their first meeting, she knew he was the right person for the job.

"After I met with him, I was like 'wow, this is somebody I want to help build a company and be successful because he's just got it,'" she said. "He has so many different ideas of how to build a company. He's like, 'How can we do it better and do it differently?'"

Making a fast run to the top has given Oakes a chance to reflect on his own leadership style, made easier by the team continuity from his days in Doudna's lab to Scribe. Empowering the right leaders is crucial to success, Oakes said, but it takes being able to empathize with their needs and wants — a callback to his psych days.

"Science is a human endeavor, and I mean that deeply," he said. "When you take that to heart as I did early on, you realize that you're only going to get out what you put in. For me, leadership is about people and building the teams and finding the ways that people tick in a way that we can be really excited about something." — *Kyle Blankenship*

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- Name **Imogen Pryce**
- Company **Relay**
- Position **VP of R&D Ops & Strategy**
- Age **38**

**Imogen Pryce brings Relay to the city**

Imogen Pryce joined Relay Therapeutics in January 2019, a few weeks after SoftBank and a few other investors cut the biotech a check for $400 million. It was the kind of deal where a company's ambitions suddenly outstripped its capacity, literally: On her first day, an HR person walked Pryce through their office and, by way of a chair and desk, pulled up a stepladder between a biologist and a chemist. "We don't actually have any space for you," the HR manager told her.

Pryce came from Shire, with its sprawling offices on multiple continents. She was tasked, vaguely, with helping Relay get off the single Kendall Square floor where, for two years, they developed new technology to let scientists watch proteins as they moved.

It was a departure from the static snapshots developers had long worked with, one that was already illuminating paths to new drugs. Eventually, though, they would have to start making those drugs. And which drugs would they make? How many? If they decided to go big and develop a bunch of molecules, how much would each cost? Would those molecules be just for cancer, or for other diseases too?

Pryce, as the new VP of strategy, presided over debates in Relay's conference rooms, whipping and directing a nerdy batch of early-stage scientists into a company that could match its own scientific ambitions. With an outsider's perspective, an insider's tongue, and a youngster's idealism, she helped draw a plan that would guide them into the clinic and toward a near-record IPO, even after Covid-19 hit

a year later.

In those first conversations, she made clear what she thought the company was. They weren't just going to do oncology.

"We can make an impact on a lot of people's lives," Pryce says she told other staff. "If we really believed that every program that we did would make the platform better and make us better as a company, then you couldn't just say, we're only focusing on oncology, it doesn't make sense, your logic breaks down. That's a place where I put my foot down."

Pryce had been thinking about the impact for a while, long before she had anything to do with the drug industry or biology for that matter.

She studied chemical engineering in college and grad school, fascinated by new technologies for solar power and filtering carbon out of the air. She left academia because she wanted to make a direct impact and she figured that, after a brief consulting gig, she'd start her own company. Her PhD work focused on technology with manifold commercial application: a kind of engineered polymer that could be turned into a biosensor to detect chemical leaks in waterways or subtle changes to an ecosystem.

At Boston Consulting Group, though, she got a glimpse into every aspect of biopharma, from merger integration to digital overhauls, and got the "healthcare bug." She liked the patient focus, she says.

Companies, in turn, liked her focus, unique for her role. Sanjiv Patel, then head of strategy at Allergan, remembered when she consulted for them on some mergers. Most consultants came in, poured over their data in a conference room, made a bunch of spreadsheets and then presented them. Patel found Pryce in the cafeteria, chatting up the company's scientists.

"I said, 'Why aren't you making spreadsheets?' And she was like, it's a waste of time, 'I can find out everything I need here,'" Patel says. "I saw that and I figured this person knows what they're doing."

Patel would soon be tapped as CEO of Third Rock's fledgling startup. For two years, he chatted up Pryce about a potential job. It was never clear, though what that job was, even after Shire — where Pryce moved in 2017 — was bought out and Pryce reported to Relay's headquarters. In the first two years, she'd rotate between official and de facto roles as communications chief, strategy, business development, financing and R&D.

Relay at the time was, like many high powered startups, effectively a large academic lab: a place of brash but cerebral scientists who could toil forever on basic science and, when asked if and when a program could get to the clinic, would reply with textbook academic caution: Maybe? We'll find out.

Pryce said yes, we'll find a way. She laid a strategy to get Relay where investors had just bet $400 million they could go. She taught senior vice presidents that they didn't have to sit in on every meeting or track every detail of every experiment, a task that often required painstaking patience and cheeky inventiveness; she'd cook up special programs that let vice presidents still have an occasional hands-on role in the lab.

She did it all without much background in biology. To compensate, every week, she pulled two scientists over to her and asked them to explain a different facet of their research. "Who doesn't feel like an imposter?" she says.

And yet no one doubted she was crucial.  Patel says scientists would talk to her and forget that she wasn't a biologist or medicinal chemist.

"If you asked most of the company, they'd say she's the glue," Patel says. "They don't know what she does but they know she's essential."

Because of her nebulous, entrenched and overarching job, it can be difficult to pinpoint the exact fruits of Pryce's labor at Relay, just as it can be difficult to nail down a CEO's. Yet there is one unambiguous marker of her time and how much she's shifted their thinking. It's the first thing you see when you walk into Relay's doors: A Playmobil set of a farm.

Pryce, in trying to explain how Relay would go from a basic science shop to a company with three drugs in the clinic and more on the way, told employees to imagine a farm. They would be a farm, she said, and at a farm, you had to protect your chickens — intellectual property — and make sure they weren't

eaten by wolves. And you had to decide, as a chicken farm, whether they also wanted to also be a goat farm. (Just oncology or also autoimmune and genetic diseases?)

“People would be like, ‘Oh, I totally get it, we need goats,'” says Patel. “It was a bizarre but simple analogy for everyone to get.”

So Relay became a farm and then a larger farm, and then ultimately, she announced last year, a city — a city with programs in genetic diseases and oncology, molecules in the clinic and one day, maybe, a commercial team.

That’s Relay’s future, but where does it leave Pryce’s? Neither Pryce nor Patel left much doubt: She would be a CEO. It was a goal for Pryce. For Patel, it was a certainty.

“One day, I’ll just show up for her work, and they’ll be like ‘Oh yeah, Imogen’s taken your job,'” he said. — *Jason Mast*

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- Name **Glenn Rockman**
- Company **Adjuvant Capital**
- Position **Managing Partner, Founder**
- Age **39**

**Glenn Rockman’s journey from the cattle farm to Wall Street**

When Glenn Rockman sat at his desk for the first time high up the JP Morgan tower at 270 Park

Avenue in Manhattan back in 2007, it was a far cry from home for the self-professed “farm boy from Michigan,” and a dream come true.

Rockman grew up with few ambitions on that cattle farm but eventually decided after graduating college that he wanted to see the bright lights of New York City — and scrape together enough cash to support himself. Just months out of school, Rockman, a Princeton grad majoring in public policy, was suddenly shipping out multimillion-dollar wires to clients. It felt surreal.

“It was hugely intimidating,” he said. “My office was almost on the top floor, and you had this sweeping view of Manhattan. It was wild.”

That initial opportunity at JP Morgan as a VP of higher education and nonprofit investment banking parlayed nearly four years later into a gig with the firm working with the Bill & Melinda Gates Foundation to determine why investors weren’t showing much interest in startups in public health and vaccines.

“The traditional venture capital industry just had no interest in picking up these assets and taking them over the finish line,” he said. “Bill (Gates) personally was frustrated because he has such an ambitious agenda for addressing every possible public health challenge out there. Meanwhile, he’s looking at all the trillions of dollars in treasury bonds, and saving accounts and General Motors stocks and asking, ‘Why aren’t more people investing in these really promising de-risked assets?’”

The rest was history. Rockman, now a founder and managing partner at Adjuvant Capital, is part of a team looking to drive investment in public health startups that have typically escaped interest because investors think they give low returns — a view he dismisses as a “failure of imagination.”

Adjuvant, financially and spiritually supported by the Gates Foundation and its philanthropic mission, officially debuted in February with $300 million in seed capital and Rockman’s vision to make smart investments that have a big impact on underserved populations. So far, the fund has placed its bets on firms like Excision Biosciences, which is working on CRISPR-based therapeutics for infectious diseases such as HIV and hepatitis B, and vaccine outfits like Yisheng Biopharma, among others.

Rockman isn’t like your normal VC. Sporting a crop of pink hair and a pink hoodie on our video call, he makes no qualms about pointing out investors’ blind spots in public health, including the possibility of sizable returns with a bit of creativity and patience.

The math, in his telling, is simple: Procurement deals for therapeutics in developing countries often funnel through a few hands, leaving a big slice of the pie for investors to jump on startups looking to join that space. Public health has left a bad taste in the VC community's mouth for years with an ROI that can't match oncology or rare disease — but that doesn't mean an investment in that space is a risky one, Rockman said.

"It's simply just telling the story to these investors about this whole world of multibillion-dollar procurement activity that the rest of the industry has no idea how to access," he said.

Jenny Yip, Rockman's fellow managing partner at Adjuvant, met Rockman nearly eight years ago when she was at the Gates Foundation and he watched over JP Morgan's Global Health Investment Fund. The two have kept a close friendship since. In her telling, Rockman's greatest strength is his "mental flexibility" and ability to synthesize and convey difficult topics between scientists and investors.

"I think he's one of those leaders that is a 'watch what I do' type of leader," she said.

This is now Rockman's third go-round working with Gates, the billionaire tech inventor and entrepreneur. In the early days of those interactions — when it wasn't exactly cool to have an investment banker advising you in the afterglow of the Great Recession — Rockman was mostly siloed off from Gates. But one story from that period stands out.

At a small cocktail hour in 2010 for JP Morgan clients, Rockman watched as Gates and a Big Pharma exec "closed the bar" after an hours-long discussion on that company's work on a malaria vaccine.

“They just debated for hours the strengths and weaknesses of only a partially effective malaria vaccine that was somewhat expensive, needed five doses and everything else,” Rockman said. “It was very clear to me that this guy lived his truth. This was his personal passion, and I saw that over and over for years.”

There’s a lot to say about working in close proximity to one of the most influential men in the world, but Rockman actually models his own leadership style off of his first boss — Diana Hoadley, then a managing director at JP Morgan and now a VP at Goldman Sachs. Early in his tenure at JP Morgan, Rockman remembers Hoadley reaching out to him, then a novice, on investment decisions.

“My very first week on the job, she was on a broad meeting with clients and she called me and asked, what do you think about this big problem?” He said. “That complete flatness and lack of hierarchy and openness to the best ideas made for the best work environment.”

Reflecting on his success, Rockman credits a two-sided approach: You have to work really hard, he says, but also be unapologetic in pursuing your passions.

“You really have to grind and suffer at the outset to get the credibility and foundational skills,’ he said. “You have to follow your passion ... but it’s hard to make that leap on day one.” — *Kyle Blankenship*

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- Name **Jake Rubens**
- Company **Flagship Pioneering**

- Position **Principal**
- Age **33**

**Gene editing? CRISPR? Yesterday's news. For Jake Rubens, the future is gene writing**

Jake Rubens always had a hunger for biology. But it took him a little while to figure out where to focus his energies.

He recalls becoming interested in research during his earliest days as an undergrad at Washington University in St. Louis. The field of biofuels originally appealed to him. Though Rubens was interested in "trying to save the world" by converting photosynthetic bacteria into oil, he turned his attention to DNA after coming across a profile of Craig Venter, one of the lead researchers on the Human Genome Project, in a magazine. He recalls stealthily reading the article while not paying attention in class.

"I think it was a huge seminar, like a 200-person seminar, and I was sitting in the back row," Rubens said. "Sort of paying attention, sort of not. Don't tell the professor that, but I don't think I got the best grade in that class either."

The distraction started Rubens down a path that led to the creation of a technology at the heart of Sana, biotech's newest darling, as well as a second company in Tessera Therapeutics, which is trying to pioneer the next step in genome editing with a platform they call "gene writing."

Once he had his mind set, Rubens started doing research at Bob Blankenship's lab at WashU, an opportunity he says he was lucky to have. Not only did the research give him early exposure to lab settings as a whole, but it also introduced him to what at the time was the emerging field of synthetic biology.

As Rubens tells it, he only became more awed by the ability this arena could have on human health. To keep "scratching that itch" and get further involved, he applied to MIT's PhD program, where he eventually received a degree in microbiology. And it was Tim Lu's lab at MIT where Rubens said he embarked on some of the most challenging work of his career, building complex genetic circuits in bacteria that could perform analog, digital, and hybrid computations.

How, then, did Rubens make the eventual shift to pharmaceuticals and biotech? While in Cambridge, he developed an interest in entrepreneurship and took every class he could find on the topic. He's now "obsessed" with fundamentally changing healthcare by eliminating genetic diseases at an early age.

"One day, we can fix disease akin to how today we can fix a broken bone, with just a single trip to the hospital," Rubens said. "And if we treat patients at a young enough age, they may never even remember being a patient at all, as opposed to that lifetime of treatment that they have today. And that's what really inspires me and keeps me going."

The end result of this was a company called Cobalt Biomedicine, later acquired by Sana in 2019. The underpinning of Cobalt's technology deals with a technology called fusosomes, which allows researchers to deliver specific molecular payloads such as gene therapies by tapping into one of the body's internal shipping and communication systems.

Rubens has had no involvement in Sana since the acquisition, though the company's meteoric rise to the largest preclinical biotech IPO ever is ostensibly in part a result of his contributions. He declined to comment on Sana beyond wishing the team well for the future.

But around the time of the deal, he had come up with his next big project in Tessera. While working at Sana, Rubens had explored different ways of approaching genome engineering and developed what he says is a templated and automated version. Rubens named the technology "gene writing" to purposely distinguish it from gene editing.

Though he heaped praise on CRISPR and said the Nobel Prize won by Emmanuelle Charpentier and Jennifer Doudna was "very deserved," Rubens said his vision for gene writing is to overcome some of CRISPR's shortcomings. Chief among those is how the technology relies on the host's DNA to repair pathways after genes have been "knocked out."

Whereas CRISPR can be used for small insertions or deletions, Tessera aims to install longer sequences with their gene writing tech. If everything works as it should, it would allow for integrating DNA into the genome without cutting it or counting on the repair pathways to stitch it back together. It could even let researchers make an AAV a permanent feature of the genome instead of acting as a satellite, Rubens said.

The strategy clearly has generated a lot of investor interest, as Tessera raised a mammoth $230 million haul earlier this year. A good chunk of the cash will go toward ramping up manufacturing and hiring new staffers — the company said in January it's looking to add 100 researchers.

For Rubens, though, everything is about science. He believes humanity could one day live in a world where chronic conditions could be treated with a vaccine, of sorts, using gene therapy. And Sana and Tessera, he says, are part of that path forward.

"There are people who can't get Alzheimer's or hypercholesterolemia because they have a mutation that prevents it," Rubens said. "Imagine if we could give those mutations to people at a young age. That sounds a lot to me like a vaccine, not for infectious disease, but chronic disease that develops from lifestyles." — *Max Gelman*

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- Name **Carol Suh**
- Company **ARCH Venture**
- Position **Principal**
- Age **32**

**It took time, but Carol Suh found her way to the business side of science — and she couldn't be happier**

Quitting her PhD program turned out to be one of the best decisions Carol Suh has ever made.

She was halfway through the program at Yale's stem cell center, studying heart stem cells, when she

realized the academic life wasn't for her.

"Academia is more about exploration and understanding the biology, and I wanted to be more a part of: How do you actually translate and commercialize that really cool science?" Suh said.

After an "eye-opening" eight-month fellowship with GSK, Suh's next steps became clear.

"I realized that I could either spend the next couple years continuing my experiments in the lab basement," she said, "or I could spend the next couple of years [working] to really understand the business side of science."

So, despite loads of advice to stick it out, Suh dropped the program and left with her master's in 2014.

"I am really glad I did," the 32-year-old said.

Now a principal at ARCH Venture, a VC firm known for its big bets, she has since gone on to help build companies like Boundless Bio, Autobahn Therapeutics, and Sana Biotechnology, driving new approaches to cancer, and multiple sclerosis, among other technologies. Sana, the first of those companies to go public, landed a whopping $587.5 million IPO this year.

"It's been a wonderful career since then," she said.

Suh's love of science came from exploring the tide pools near her childhood home in Rancho Palos Verdes, CA. They inspired dreams of becoming a marine biologist, then a meteorologist, then a

geologist — you name it.

Her love of science persisted through middle school, when she entered her first science fair, and into high school, when the 14-year-old would spend her weekends conducting research alongside grad students and postdocs at UCLA. She lived about an hour away from campus, and her parents would drive her each way.

“I’m very thankful to have them take a chance on the high school student,” Suh said. “That’s where I first started researching stem cells and fell in love with the field.”

She went on to Harvard, where she worked in David Scadden’s lab at the school’s stem cell institute. They were focused on understanding how factors in the bone marrow influence how stem cells differentiate and specialize.

After graduating with her master’s from Yale, Suh found herself working as a senior associate consultant at Trinity Partners. She wanted a “crash course” on the business of science, and that’s what she got.

“Trinity Partners was a really great way for me to learn how different biopharma clients, big and small, think about problems like corporate strategy, indication prioritization, thinking about forecasting, etc.,” Suh said.

With a nagging feeling that she still needed more training, Suh applied to business school. But around the same time that she was accepted to Stanford University, she got an interesting offer from a Third Rock recruiter. The VC firm was launching a stem cell company, helmed by Suh’s former boss at GSK, Jason Gardner, and co-founded by Scadden, Suh’s undergraduate research advisor at Harvard — and they wanted her help.

While hesitant at first, Suh thought the opportunity was too good to pass up. “It was almost in a sense, the universe was telling me to do this,” she said.

She put off business school for a couple of months to help Scadden launch Magenta Therapeutics — her first foray into company building. The startup nabbed a hefty $48.5 million Series A back in 2017, then priced a $100 million IPO the following year.

She fell in love with the launch phase of startups. “You’re with about five people, incubating in an office that’s supposed to fit two,” she said, “and you’re just really excited about the mission and vision of the company that you’re starting.” With Stanford calling, Suh returned to the West Coast. She kept in contact with Magenta and helped out part-time while pursuing her MBA. Then in her second year of business school, she connected with ARCH.

Jumping from industry to VC wasn't a decision, per sé. "I really sort of stumbled into it," Suh said. "I just knew I wanted to be a part of early-stage, innovative biotech companies."

She graduated from Stanford in 2018, and officially joined ARCH that same year. While working her way up from consultant to senior associate to principal, Suh's job has varied from company to company. In the early stages, it's typically about evaluating the science and weighing opportunities. Then it's strategizing.

Already, she's helped launch three companies, relishing the chance to work at a firm willing to bet big on potentially transformative technology. And, she said, there's much more to come.

"My favorite things that I've worked on are actually the ones still probably in stealth mode right now," she said. — *Nicole DeFeudis*

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- Name **Christina Trojel-Hansen**
- Company **ARCH Venture, Oscine**
- Position **Entrepreneur-in-Residence**
- Age **38**

**Christina Trojel-Hansen follows her nose across continents, and to the biggest startup in biotech**

On a cool fall day a few years ago, Christina Trojel-Hansen biked from her apartment to Copenhagen University, where a balding, brilliant and kind-spoken neuroscientist waited with a laptop full of years

of published and unpublished data.

Steven Goldman knew industry. He had worked over 3 decades with Merck, Biogen, Sanofi and others, even once agreed to co-found an ill-fated startup. It's why he didn't trust industry, not with his life's work at least. He needed to know that it wouldn't get shoved aside if there was some change in leadership or investors wanted a new direction. He had already turned away about a half-dozen offers.

Trojel-Hansen didn't have the pedigree or resources those companies brought. She had barely been at Novo Seeds for a year and only as a senior associate. But she believed that cell therapy could transform medicine and, over two hours that day, she convinced Goldman that she would fight to advance his research: a form of implanted, lab-grown cells that might treat deadly neurodegenerative diseases, including Huntington's and multiple sclerosis.

"Here's a young VC who walks in the doors not unannounced, but with very little background, and she seemed to have more understanding of the science and the background than most of the folks — almost any of the folks — I had dealt with previously," Goldman says. "She convinced me."

Neither Trojel-Hansen nor Goldman understood where that decision, his science and her uncompromising conviction would take them: down an intercontinental rabbit hole to one of the flashiest names in biotech investing and, through them, to a stealthy behemoth that would raise nearly a $1 billion in an effort to reimagine cell therapy. It would get Goldman the funding and autonomy he needed and, after quitting her prestigious job to run a fledgling startup, turn Trojel-Hansen into one of California biotech's busiest serial entrepreneurs.

They ended up in the US in large part because Trojel-Hansen got fed up with European investors. An instinctually cerebral scientist who had studied epigenetics at Berkeley and mitochondria at the Gustave Roussy Institute in France, she found Goldman's work through her own PubMed carousing. She felt transfixed when the scientist laid out the work in full.

"He opened up his computer and it was like opening Pandora's box," she says. "Research I've never seen so solid and so much of it at the same time."

European investors, though, didn't agree. Cell therapy was still new; the first CAR-T treatment, Kymriah would only be approved that summer. The VCs poked holes in their plans. They asked how much we actually knew about cells and whether they could ever be manufactured at scale. A syndicate started to form but it didn't match what Trojel-Hansen believed they needed to put Goldman's cells into the clinic.

So, with Goldman's gentle encouragement, she quit her job at Novo, became CEO of the company, Oscine, packed it up from Denmark and moved it to Rochester, NY, where Goldman also taught. She spent $30,000 of her own money flying between and across continents to convince investors.

"It was tremendously courageous on her part," Goldman said. "She walked away from a steady job and came into the US with no real record."

Trojel-Hansen, for her part, was mildly terrified. Not only was she now working in a nascent field with few outside experts to turn to and virtually no little knowledge or experience besides her own obsessive reading, she was also now a first-time CEO in a new country.

"I was like, 'Oh boy, what did I do here?'" she recalled. "Then I had to go ahead with the fundraising. I had to figure it out on my own, all of it. And I had to align myself with good people that I could ask. It was like a new world that opened up for me, totally exciting but also super scary."

Through a series of acquaintances, she eventually met Bob Nelsen, the idiosyncratic ARCH Venture managing director behind the big cell therapy startup Juno and a long lineup of other gaudy startups. Nelsen recognized the potential of their tech, and put Trojel-Hansen in touch with the cell therapy 2.0

startup he was now incubating with Flagship, a behemoth that would eventually become known as Sana.

Sana's CEO Steve Harr and chairman Hans Bishop flew out to Rochester, where Goldman had a teaching position and Oscine had set up shop. Trojel-Hansen, always protective of their science, negotiated a deal that would allow them to scope out Sana and know they were truly committed to advancing their brain cell transplants before moving ahead with a full acquisition.

Last year, she got a call again from Harr. Goldman's cells were nearing the stage where they could be tried in humans, and he wanted to incorporate Oscine fully into Sana, which would soon go public at a valuation of over $4 billion. Still, Trojel-Hansen and Goldman drove a hard bargain before saying yes.

"It was very important to both of them that they had confidence we would fully invest in understanding the potential of the platform," Harr recalled. "That was one of the things they were very transparent about."

Goldman stayed with Sana to shepherd his cells to the next stage, but Trojel-Hansen turned down their offer. Even as Oscine CEO, she had been laying the groundwork for her next moves, seeing glimpses of exciting science online or at conferences, following it down rabbit holes and teaming with top researchers to begin gaming out companies.

She is already working on four different new companies spanning four different technologies, including drugging mitochondria and editing the epigenome, the series of tags and binders that govern how genes are expressed. It's work that tacks back to the research she conducted at Berkeley over a decade ago.

One day, she said, she'd like to take a prominent CEO gig and stay to guide a young company to success. She's not sure, though, whether she'll ever be able to stop following her nose for the next big thing.

"I'm not sure I can stop having these company creation ideas," she said. "As Steve Jobs said, 'Stay hungry, stay curious.'" — *Jason Mast*

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- Name **Laura Walker**
- Company **Adagio**
- Position **CSO**
- Age **36**

**Laura Walker ditched academia for biotech — and now heads science at Adagio**

Laura Walker had a choice to make.

Growing up a fly on the wall in her scientist father's lab in Princeton, NJ, one thing was clear: As a researcher, you don't go work for the industry. But during a short stint as a postdoc at UCSF studying B cell immunology, Walker found herself weighing a move out of academia and into corporate biotech.

It wasn't an easy decision to make, but Walker knew that her work in virology could translate well to the right company. And, ultimately, she was looking for an environmental change in a big way.

"I found it to be a very stressful place to be in part because there isn't very much funding now," she said. "I remember my dad hated industry — he used the word 'toxic' and (said) scientists in the industry couldn't cut it— so I was really conflicted about doing that. But I did."

That's the story behind how Walker, a University of Wisconsin-Madison biochemistry graduate and veteran of the Scripps Research Institute, found herself at Lebanon, NH-based Adimab in 2012 under the leadership of serial biotech entrepreneur Tillman Gerngross and eventually as co-founder and chief scientific officer at spinoff company Adagio, toiling away on Covid-19 antibodies.

But Walker's journey began back in her father's lab, where she saw firsthand the way that research is

carried out. Before her head ever reached bench level, Walker was hooked and had a clear line of sight on what she wanted to do.

“I guess I wanted to be in science as long as I could remember,” she said. “My mom has this quote from me from when I was three saying I want to be a science guy. Funny that I said guy because I only probably only saw men in the lab.”

That drive to return to the lab led her first to UW-Madison and then onto Scripps, where she worked with Dennis Burton and his team on broadly neutralizing antibodies for HIV. Burton is a recognized expert in the space, and Walker recalls her time there mostly for the hothouse environment working on cutting edge HIV research and also Burton’s example in taking time to consider the big picture.

“I remember we were sitting in his office one time and he said, ‘You know, we’re really paid to think here,’” she laughed. “I spend a lot of my time feeling a little guilty that I’m thinking too much and not doing enough, but that made me feel better.”

The next step after Scripps seemed obvious to Walker — chasing a postdoc — and she chose UCSF in order to study B cell biology to help flesh out her other research in viral immunology. But almost immediately, Walker began to regret the decision. Her lab was constantly chasing funding, and she found the environment extremely tense, unlike the more collegial atmosphere in Burton’s lab.

After putting out some feelers, Walker ended up taking an offer at Adimab in 2012. The antibody discovery specialist at that time was pretty small potatoes, but Walker had previously worked with then-CSO Dane Wittrup back in Burton’s lab and saw an opportunity to fit in well with the company’s yeast library concept. That trajectory put her in the orbit of Gerngross, who was by that point a well-known biotech entrepreneur and a bit of an eccentric — Walker says he takes time to buzz around on his dirt bikes and owns his own lighthouse. She also found him to be an extremely effective leader and a good example for her own leadership style later on.

“I haven’t worked at other companies, but I have to think that he’s one of the best CEOs in the world,” she said. “He is this interesting combination of brilliant scientist and brilliant businessman, and that’s exactly what you need in a good CEO. He cares so much about the people that work for him; he just genuinely cares about everyone’s wellbeing.”

After taking on the director of antibody sciences role at the firm in 2019, Walker seemed poised to keep growing her responsibility at Adimab, but that path, like so many other things, was disrupted by Covid-19. Early in the pandemic, Gerngross envisioned an Adimab spinoff that would focus exclusively on neutralizing antibodies for SARS-CoV-2.

That was the concept behind Adagio, which launched in April 2020 with Walker heading the science from Adimab's offices. The company wasn't one of the earliest players with antibodies in the clinic — in fact, the biotech's just recently dosed its first patients — but Walker has reason to believe her team's molecules could crack the code on what has been a mixed showing from big drugmakers' antibodies across the board.

Launching a startup in the middle of the pandemic hasn't been easy, Walker says. The team has been completely virtual since day 1 and has been in a race with bigger drugmakers to churn out results. Leaning on the Adimab connection, Walker's team published its first results in *Science* as early as July and started dosing its first human patients in February.

"It was very chaotic, especially at the beginning, because of all the uncertainty around the virus, and just the conditions here at Adimab," she said. "It was probably the fastest my group has ever done anything. It's this feeling of working together to what feels like save the world — coming into work every day was really exciting."

Meanwhile, Walker also has the chance to hone a leadership style she thinks is a blend of the examples from Burton, Gerngross and her mother. Walker's a real bench scientist and admittedly hasn't spent much time considering her thoughts on being a leader, but she likes to start from a place of empathy

with her team.

“I’m a relatively sensitive person — I’m a sponge, and I can pick up people’s emotions,” she said. “I really care about everyone in my group, and of course I want to maintain high-caliber science.” — *Kyle Blankenship*

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