Masters of Scale: Rapid Response Transcript – Reshma Shetty

"The promise and peril of engineering biology, w/Ginkgo Bioworks Reshma Shetty"

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> **RESHMA SHETTY:** This pandemic was going to define how people thought about biotechnology for the rest of their lives. Biotechnology could either be something that people were afraid of, or it could be thought of as something that helps provide the tools for fighting back.
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> Our mission at Gingko is to make biology easier to engineer. We, in the next decade, can have huge beneficial impacts to our food supply and how we grow and make our food, to our health and how we treat disease, to our environment, to how we treat multidrug resistant infections. Let's go make this happen. Let's show the world what's possible with biology.
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> When the pandemic came to Boston in March of 2020, it really hit home for us. Nobody had actually stood up mRNA vaccine manufacturing at scale. And so we launched a set of programs around mRNA vaccine manufacturing, including our collaboration with Moderna to help try to drive down the cost and drive up the scale, importantly. The technology we're working with is so important. This is not social media, this is not advertising. This is your life, this is our community, this is our food supply, this is our environment.

BOB SAFIAN: That's Reshma Shetty, co founder and COO of Ginkgo Bioworks, the breakthrough synthetic biology company.

After pivoting to Covid-19 response efforts in 2020, Ginkgo recently announced plans to go public via SPAC acquisition, at a reported $15 billion valuation.

I'm Bob Safian, former editor of Fast Company, founder of The Flux Group, and host of Masters of Scale: Rapid Response.

I wanted to talk to Reshma because biotech could be the next engine of global innovation. And Gingko has a platform that serves a wide range of industries, from food and agriculture, to materials, to health care.

Biotech and Gingko enabled the vaccines that are beating back Covid-19. Yet Reshma acknowledges that the stakes in engineering genes are extraordinarily high, for her business and for all of us.

She stresses the need for what she calls an unstable equilibrium in biotech development, to pair the ambition of Silicon Valley with a higher level of care.

[THEME MUSIC]

SAFIAN: I'm Bob Safian, and I'm here with Reshma Shetty, co-founder and COO of Ginkgo Bioworks. Reshma is joining us from the Ginkgo offices in Boston as I ask my questions from my home in Brooklyn. Reshma, thanks for joining us.

> **SHETTY:** Thank you so much, Bob, for the invitation to be here.

SAFIAN: So, first of all, congratulations on the recent announcement that Ginkgo will be going public via a SPAC later this year. It's very exciting. $15 billion valuation. It's kind of a coming of age moment for synthetic biology.

> **SHETTY:** I think that's right, yeah. I first started in the field back in 2002 when I was a first year graduate student at MIT. And there, I met Tom Knight – who later became my co-founder – and he really inspired me with his vision of being able to program cells the way you program computers, and fell in love with it. Fortunately, I was a naive grad student and had no idea how hard this was going to be, but that's what makes it fun.

SAFIAN: So for those less familiar with the term synthetic biology and with Ginkgo, can you describe what you do and what your platform provides?

> **SHETTY:** Yeah. Here at Ginkgo, we essentially program cells much the way you program a computer, right? So it's sort of hard to believe but at its core, biology is fundamentally digital. It's made up of As, Ts, Gs, and Cs. That's the DNA of your cells. The food you eat, the microbes in your environment, they all have genomes made up of As, Ts, Gs, and Cs. And if you change the order of those As, Ts, Gs, and Cs, rewrite them, edit them, flip a base here or there, then you can introduce whole new functionality into the cell, change its behavior, and much like you would write a computer program. And so at Ginkgo, we've basically been working for the last over 10 years now to make the process of editing DNA, rewriting DNA easier.
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> In some sense, you can think of what Ginkgo does as building the editor compiler and debugger for biology. So you want to be able to write code, you want to be able to edit that code, and you want to be able to compile it into actual DNA that you put into cells, and then you want to be able to see how those cells work and debug when things go wrong.

SAFIAN: And so other organizations come to you to say, "Hey, I'm looking for a cell that can do this." Or, "Can you help my food cell be different, or my material cell be different?" Is that what's happening?

SHETTY: Customers come to us and they might fall into one of a couple of different categories. So some of them are super sophisticated about cell programming, right? They might have capabilities in house, and they already know, hey, I want to make this molecule at this level of production and I want it to cost this much in my commercial scale production process. Other customers are much less sophisticated about cell programming or more like, "Hey, this is my business, and I have this set of problems, and I was thinking that maybe biotechnology might be useful. Is there any relevance to any part of my business?"

And we talk about the problems they're facing and how biotechnology might be able to help. Maybe they're having supply chain problems, maybe they need a new functionality, a new material, maybe they really want to drop their cost of goods.

SAFIAN: So when the pandemic hit, a lot of folks in the sciences looked for ways to respond, designing ventilators, or tracking data with new apps, right? I know you guys ended up working with Moderna on their vaccines. You also looked at therapeutics and the testing. How did Ginkgo go about getting involved?

SHETTY: When the pandemic came to Boston in March of 2020, it really hit home for us. And what struck us here at Ginkgo was that, hey, biology was suddenly having this dramatic impact on everybody's lives. And that this pandemic was going to define how people thought about biotechnology for the rest of their lives. Biotechnology could either be something that people were afraid of, or it could be thought of as something that helps provide the tools for fighting back.

And we realized that in order to have an effective pandemic response, it was going to need to be a multi-pronged approach. We're going to need to be able to test and isolate people who have COVID, we needed to be able to find therapeutics to treat people who are already sick, and we needed to be able to come up with vaccines to prevent people from getting sick in the first place. And so, although we weren't very active in infectious disease at the time, we felt like we had, in some sense, a moral obligation to figure out how we might be useful in pandemic response. And so, yeah, we launched essentially a bunch of experimental programs to see how it might be useful. We realized that mRNA vaccines, like the ones that Pfizer and Moderna worked on, were going to be potentially a very interesting solution, but we also knew that they were going to be manufactured for the very first time.

So assuming you found a vaccine that worked, nobody had actually stood up mRNA vaccine manufacturing at scale. And we knew a lot about how to make some of the precursor components for mRNA vaccines, we knew a lot about how to make some of the enzymes that are needed in mRNA vaccine manufacturing. And so we launched a set of programs actually around mRNA vaccine manufacturing, including our collaboration with Moderna to help try to drive down the cost and drive up the scale, importantly, of mRNA vaccine manufacturing for the world, and those are programs we continue to work on today.

SAFIAN: And when you were looking at these different options, was there a group of you that got together, and you sort of divided up who's working on vaccines and who's working on therapeutics?

SHETTY: I mean, we essentially almost did a lean startup, right? Hypothesis building and figuring out if there was something we could do over the course of the next three months. And some ideas fell by the wayside, but others really took flight. And the two in particular that really had legs for us were around mRNA vaccine manufacturing, and then the second was actually around K through 12 testing.

SAFIAN: And so that latter testing effort, that's something that's continuing to persist now, even though vaccines are proliferating? A lot of younger kids aren't eligible to get vaccines yet.

SHETTY: That's right. I have two kids, a lot of folks out there probably have gone through a lot of pain over the last year where their kids might not be fully in school or might not be in school at all. And the question we asked ourselves is, hey, how can we help support school reopening? And so most of the folks who are thinking about COVID testing, particularly early in the pandemic, were entirely focused on diagnostic testing, which makes sense. We had a bunch of people who were sick, we needed to know who was sick and who wasn't and helped to diagnose cases. But when we started thinking about schools and what they needed to be open safely, we realized that diagnostic testing wasn't the right tool. First of all, it was just way too expensive.

Typical diagnostic test is $100, $150 a test, right? How are you going to administer a $100 test to every kid in a school? It's just way too expensive for public schools to be able to afford. And second of all, it was just way too logistically intensive. You're not going to be able to get a doctor or a nurse to be able to administer this test to every kid in a school. And even today, right? As you said, kids under 12 aren't eligible for vaccines yet. And so we still have to worry about the spread of COVID amongst those who aren't able to be vaccinated. And so we had to really reconceptualize COVID testing and think about it, not from a perspective of diagnostics, but rather from the perspective of public health. How do we help survey what's going on at a school and know whether or not there's an outbreak happening?

SAFIAN: And so how does that look different?

SHETTY: Well, first of all, you want to be able to test every student, right? Just testing a handful of kids or just the kids who are symptomatic isn't enough because we know that COVID spreads asymptomatically. Second of all, you want to be able to do it quickly. And so the idea that we and others came up with was the idea of doing what we call classroom pool testing.

And so what we do is essentially just take a little tube, we have it in the front of the classroom in a coffee mug, and each kid can basically take a swab and swab themselves and drop it into that tube. And so you test the entire class of kids, up to 25 kids plus a teacher, all at once in a single test. And so instead of spending $100 or $150 per test, you spend $100 or $150 per classroom, which dramatically reduces the cost of testing. And kids as low as kindergarten can do this test. We actually piloted this with my first grader at her school.

And it was really fun to watch them. The principal texted me afterward and said that one kid was really sad that they didn't get to participate because their parents hadn't given the consent. And so she actually started crying because she didn't get to participate in the class COVID test. But we found it was actually really easy for teachers to do this because each kid could do it themselves, drop it in the tube, then you just cap the tube and mail it in, and you can then test the entire class all in one shot. And so it's a way for schools to be able to test every student every week.

SAFIAN: And so this isn't necessarily a scientifically different way of testing. It's just a procedurally different way.

SHETTY: One of the things we realized was that we didn't need a new testing technique. We actually have plenty of COVID testing lab capacity now that we've built up over the last year. What we needed was a different way of collecting the samples. So this was as much a logistical challenge as anything else. And so we thought about everything from having kids spit in a bucket and testing the spit to sending kits home with families, and none of those ideas really could we see panning out as a way to do nationwide testing. But this idea of collecting a bunch of swabs in a single tube and having a tube per classroom, it's really scalable.

And so now we're offering statewide testing in Massachusetts and in Maine and in Maryland with a couple of counties there, like Baltimore.

SAFIAN: There's been a lot of discussion over the last year about the accelerated adoption of technology, not necessarily an advance of the technology itself but just more adoption to it. In terms of science, in terms of bioscience, is it the same pattern? Is it heightened adoption of the things you already had in place, or has there been heightened development too?

SHETTY: I think there's been a mix of adoption of existing technologies as well as new technology development. So mRNA vaccines, for example, folks have been working on those technologies for a long time now. But COVID really brought the need for those on a worldwide scale into stark relief. So that's obviously a massive adoption that's happened, but if you want to be able to make these mRNA vaccines at a scale that you can administer two doses to every single person on the planet, obviously you need a ton of technological advancement on the manufacturing side. So I would say the adoption has actually driven the technology investments and development.

I think what the pandemic has brought home for people is, one, biology is really important. It's core to our lives, it's core to our health, it's core to our food, it's core to our environment. And it's also brought home just how powerful these technologies really are.

SAFIAN: So as COO at Gingko you're responsible for company building and scaling as the rest of the scaling of bioscience is going on. You mentioned to me that the approach and culture is different in Boston than in Silicon Valley. You told me, "'Move fast and break things' doesn't work for us." Can you explain that?

SHETTY: Yeah. When you are working with as fundamental a technology as biology, it really requires a lot of care. Thinking about the implications of this technology, how it gets adopted, who it benefits, and bringing a level of quality and rigor to the work is super important. And so when we think about building a company in Boston around biotechnology, I think there are a lot of really great lessons that we can adopt from Silicon Valley technology companies, but we also have to do things a little bit differently just because the technology we're working with is so important. This is not social media, this is not advertising. This is your life, this is our community, this is our food supply, this is our environment.

SAFIAN: So you're talking about the risk of unintended consequences, right? Are you talking about this for business reasons and regulatory reasons, for moral, ethical reasons?

SHETTY: Our mission at Gingko is to make biology easier to engineer. And so we want to be able to make these technologies accessible and available to improve human life. But if you're going to make these technologies more accessible, if you're going to open up the application space, you need to think about what applications are you going after. And you need to think about who stands to benefit and who doesn't. And so we don't pretend to have all the answers, but I think we realize that in the past people pretend or believe that the technology itself can be value neutral, that you can just be a platform company, and not be an arbiter of who gets to use or develop your platform – we don't feel that way about our platform for engineering biology.

We're building a platform for cell programming, and the people who develop and use that platform have a huge influence on how it gets deployed and who benefits from it. And so I think developing a culture around care for that platform and how it gets used is super important to us. And I think one of the things we find is that these are not easy questions to answer. And so oftentimes what we're trying to do when we build the culture at Ginkgo is build what we think of as unstable equilibriums, trying to strike the right balance between ambition and care, or the right balance between exploring the full potential of biotechnology but also being thoughtful about where it gets deployed.

SAFIAN: So it’s, you say unstable equilibrium, like you want to have a balance there but you don't want it to be a steady state. You don't want it to be static. The rules can't be too rigid?

> **SHETTY:** Yeah. So what is an unstable equilibrium in physics? An unstable equilibrium basically means the position of an object is a point where if it deviates a little bit on either side away from that position it's in, it'll move further away from the position. And so I think a lot of companies tend to end up in steady states that are not optimal. So as an example, a lot of technology companies, they end up in one of two steady states. They tend to be a small, very scrupulous, careful company where they never overstate what the technology can do. They're super rigorous, they're careful, but they never manage to grow to a state where they're really impacting the entire world.
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> On the other hand, there's an equally comfortable steady state that companies can end up in where they're high growth, they're super flashy, they're making all these big promises, selling a big dream, but they don't have the science and engineering to back it up. And so the question is, how do we at Gingko achieve an unstable equilibrium and where we are being careful and rigorous and scrupulous about the science, but we're also painting the picture of what this technology can do, where it can go, so that we can capture people's imaginations and help them see and realize that future opportunity?

SAFIAN: And does part of that balance end up being that there may be clients who come to you who ask you to do certain things or have certain goals and you're like, "Yeah, we could do that, but we're not going to"?

> **SHETTY:** I think that is a possibility. I think usually with the applications that folks want, it's not so black and white of, "Oh yes, we should do this," or, "No, we shouldn't." It's more that we need to think about the implications of what's going to happen and think about how we hopefully ensure that these technologies are used overwhelmingly for constructive purposes. So it's more about shades of gray.

SAFIAN: So you also mentioned to me this phrase, unstable equilibrium, talking about the workplace at Ginkgo and the challenge between workplace discussion and engagement on political issues and social issues and areas of potential divisiveness.

> **SHETTY:** I think a lot of companies are sort of struggling with how you handle workplace discussions of controversial topics, right? So whether it's politics, religion, social justice issues, diversity, equity, and inclusion, right? And again, I think a lot of companies tend to relax into one of two steady states. Either they say, "Hey, we're going to follow the Coinbase and Basecamp model. We're just going to forbid any non-work-related discussion at work because at work people should be focused on work, and we don't want to have the distraction of these other conversations." Or on the other hand, other companies end up in a different steady state where they say, "Hey, we believe in free speech. Anybody should be able to say whatever they want.

We're trying to be thoughtful about these issues. How do you achieve that unstable equilibrium in which people can focus on the mission, right? Because the idea that companies can somehow remain completely divorced from the political issues or the social justice issues that are surrounding them, I think is, candidly, a little bit naive. And so you need to strike the right balance. Enabling focus on the mission, but also enabling people to bring their full selves to work and talk about the issues that affect them in their day to day lives and candidly, even their work at Ginkgo.

SAFIAN: Research science historically is made slowly, patiently, years of work, gradually building to things. Does it still work that way? Does having that part of your culture differ also from Silicon Valley where people are trying to iterate and produce new releases every week sometimes?

I think one of the challenges with biology in general is that you can only iterate as fast as the life cycle of an organism, right? You have to grow it. It has to replicate. And so while there are certainly some parts of our platform where we can iterate very, very fast, there are also others where it just takes time and long-term investment. One of the things we think about a lot is how do we strike the right balance between short-term wins and those long-term investments that other companies might not have the patience for. And so sometimes we certainly have found that some of the biggest frontiers and new advances that we've made come from just a first principles, blind faith bet on the future. As an example of this several years ago we actually made a commitment to buy, at the time, 10 megabases of synthetic DNA.

And at the time I think the biggest consumer of synthetic DNA was probably a tenth of that, maybe less. And so we said, Hey, we're going to place an order for 10 times the amount of DNA over the next year and just figure out how we're going to use it, right? And there was no expressed customer need for that, but we knew that both to advance the technology and to change the scale at which we were engineering biology, we needed to make that investment. And that sort of forward-leaning bet led to the development of a bunch of technologies. And we were able to then, in subsequent years, drive that to 100 megabases of synthetic DNA and even beyond today. And so those types of bets are sometimes ... They're not justified if you pencil them out. They're not justified by any sort of financial model, but they're leaps of faith that you make to help drive the technology forward.

SAFIAN: That kind of basic science research used to often revolve around government funding, not coming out of a private organization.

SHETTY: I think in this country we actually do have a long history of companies investing in long-term research. We have the Bell Labs, IBM Research. We do have a history of that. But I think you're right, that in more recent years, that type of long-term focus has been left primarily to academic labs and government labs. And to be clear, they play a super important role. The reason we started Ginkgo is we felt that there were a set of problems and a set of things that we could do in a company setting that we couldn't do in an academic lab.

So we can assemble a large team of people that are a mix of software engineers, automation engineers, chemists, biologists, geneticists, chemical engineers, mechanical engineers, you name it, and all work on a common problem together, right? And so I think there are certain problems that really lend themselves to being done in a company where you can marshal a big set of resources and a huge diverse team of people towards a common goal.

SAFIAN: There's some folks who are worried that in places like China, the government or other companies are pursuing certain kinds of bio-science work that may not be held to the same kinds of science standards. Is that a competitive environment that you have to worry about?

SHETTY: So the interesting thing about biology is that it's everywhere, right? And the tools for engineering and biology are pretty ubiquitous. So there are labs all over the world who have access to molecular biology tools. It's not trivial, right? Not just anyone can do it, but it's certainly very, very international. And so I think when you then start to think about biosecurity and what does that mean, it means that we can't take the same approaches that we've taken for, say, nuclear technologies.

With nuclear technologies, you can have a hope of, sort of, locking them up and restricting access. That doesn't work for biology, right? And similarly, if you think about the rise of the internet, I think we were candidly, as a society, slow on the uptake to think about cybersecurity. We pioneered the technology and advanced the technology, and we didn't build in security along the way. And I think one of the lessons from COVID, but that we were thinking about even prior to COVID, was, as you build the tools for engineering biology, how do you build in some biosecurity along the way? It's not an easy question and it's not an easy thing to do, but I think one of the answers is that the very tools that we are building to make biology easier to engineer are also the same tools that you can use to respond to biosecurity issues. And that's what we've seen with the COVID-19 pandemic. This is a public health crisis, and there are a set of tools that biotechnology can offer to provide different layers of protection. Our testing is coming from the enzymes that were able to make PCR tools for detecting these viruses. Our therapeutics are coming from the antibodies we can engineer to help treat viral infections. Our vaccines are coming from mRNAs and other types of technologies that we've been investing in and developing for decades now.

So it's very clear to me that the best security we can offer is a very rapid response defense. That is our best protection against these types of things, whether the threats are natural or engineered. So running fast, investing in biosecurity, is I think an important thing for every nation to be thinking about. And in particular, I think COVID has shown us that biosecurity is not just important in its own right, it also ends up becoming fundamental to the economy itself.

SAFIAN: What's at stake for Ginkgo right now?

SHETTY: We built a 500 person organization that's entirely focused on this goal of making biology easier to engineer. And I would say that from my perspective the opportunity we have in front of us, both via the SPAC transaction and the additional resources that that's bringing to the table, as well as, just the opening the COVID-19 pandemic has provided in raising everyone's consciousness about the importance of biotechnology.

I think that we, in the next decade, can have huge beneficial impacts to our food supply and how we grow and make our food, to our health and how we treat disease, to our environment and how we clean up the messes we've made in the past, to how we treat multidrug resistant infections. There are just so many opportunities here for biology. And to me, the critical thing for Ginkgo is, let's go make this happen. Let's show the world what's possible with biology.

SAFIAN: Well, Reshma, this has been great. I really appreciate you sharing all of this with us. Thanks again so much for joining us and sharing your insight and your experience. We really appreciate it.

SHETTY: Thank you.