Masters of Scale: Rapid Response Transcript – Francis DeSouza

“How mission fuels risk-taking”

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BOB SAFIAN: That’s Francis DeSouza, CEO of Illumina, the world’s dominant maker of gene sequencing technology

DeSouza is locked in a battle with the FTC over the re-acquisition of a company Illumina previously spun out, called GRAIL, that has a breakthrough cancer screening test.

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 with Francis because Illumina has been a critical driver of Covid vaccines and other extraordinary bioscience advances.

Yet to keep on the cutting edge of innovation, he’s had to embrace ongoing risk-taking, even at a public company with a $70 billion market cap.

And that risk taking has led to unexpected conflicts, including with the government.

The Grail deal offers a peek into the myriad levers that help to accelerate scale, for a company, and for an emerging industry and technology. To cultivate a new marketplace, DeSouza has delved into both research and deal-making, and he offers a personal reflection on the lessons and reality of grappling with regulators.

What underscores his entrepreneurial efforts is a passion for Illumina's mission: improving human health by unlocking the power of the genome.

When your mission and your business model are aligned, the hard decisions – about risk, about investment, about priorities – become simpler and clearer. It's an approach that all business leaders can rely on.

[Theme music]

SAFIAN: I'm Bob Safian, and I'm here with Francis DeSouza, the CEO of Illumina. Francis is coming to us from his home in San Francisco, as I ask my questions from my home in Brooklyn. Francis, thanks for joining us.

> **DESOUZA:** Thanks for having me, Bob.

SAFIAN: So, it's been quite a year for biotech, genomic science, gene sequencing, highly effective mRNA, COVID-19 vaccines rolling out, something Illumina has played a part in, which is great. You're also in the midst of trying to reacquire a company that was spun out of Illumina, GRAIL, for about $8 billion. You face some regulatory hurdles here in the U.S. and in Europe. So, many good things, some challenging ones.

I want to start with a general question. There's often a perspective for entrepreneurial leaders, particularly out of Silicon Valley, that in order to maintain innovation and to scale while challenging traditional models and institutions, that it's better to ask for forgiveness than to ask permission. The health and biotech arena is a little different, but how do you think about that idea of permission versus forgiveness in the way you drive toward innovation?

> **DESOUZA:** I think there are some really important differences between healthcare and tech. Primarily, one of the biggest differences is just the stakes, right? For what you do in healthcare, you are directly impacting the lives of people. And so, we feel an incredible sense of urgency. You can actually impact lives more quickly.
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> Having said that, you also want to move carefully – and you want to make sure that you've done all the right things, such that what you put in the market is actually helping and not hurting. Doing the work around the studies, doing the work around the regulatory approval. And then also, the way healthcare is set up, you need to do work with the reimbursement entities to make sure that they have the data such that an innovation you bring to market is actually accessible to the community, Reached by the communities

that you intend to help. And so, we share the sense of urgency, but I think there's more work that gets done in healthcare before an innovation comes to market, and rightfully so.

SAFIAN: Illumina has worked successfully to get FDA approval for various innovations and to get the payment systems all in place.

Now, this deal with GRAIL has put you in conflict with a different part of the government, with the FTC, the Federal Trade Commission, as well as with European regulators. Can you explain to us how you find yourself in this situation?

DESOUZA: Illumina, for the first decade plus of our existence, we used to sell genomic analysis tools into the research market. And then in 2013, we entered the clinical market for the first time through the acquisition of a company called Verinata that did noninvasive prenatal testing.

Now, the way GRAIL started was, we were processing samples from pregnant mothers in our noninvasive prenatal testing lab. One of our scientists, this incredibly brilliant woman, noticed that although the fetal DNA in the blood was normal and healthy, there was something unusual about the maternal DNA. And so, she alerted us, we alerted the doctors to say, "Look, something seems to be off with the mothers here." The doctors got back to us and said, "No, all the moms are fine, but we'll stay in touch with them and see how they do." In all of those cases, the mothers went on to find that they had cancer and didn't know it.

I remember clearly the meeting at Illumina, and I still get goosebumps when I think about it, where we realized that we could be seeing the signals of cancer in a blood test. And so, we quickly put a team on it in Illumina. This was in the 2014, 2015 timeframe. They worked for over a year and came back and said, "Yeah, it looks like we're seeing signals for cancer, but there is a lot of work that needs to be done between where we are now and actually having a safe test that we can bring to market. We need to do some very large clinical studies, and we need to hone the test to understand what specifically are we looking for in the blood."

We knew that would take huge investment, and so we spun out the technology into a company called GRAIL. We put over 40 Illumina people into GRAIL, and we raised, ultimately, over $2 billion. And that's one of the reasons we wanted to spin it out, to get access to the capital to move this technology as quickly as it could.

The GRAIL team worked for a few years, and in the fall of 2019, they published their results. And the test they developed is truly extraordinary. This is a blood test that can identify 50 types of cancers across all stages.

Now, we know cancer kills 10 million people a year around the world, 600,000 here in the U.S. alone. We also know that if you catch cancers early, the patients have a much higher chance of survival. In a lot of cancers, you'll see the odds of survival can get higher and up to 90 plus percent if you catch it in stage 1 or stage 2. The challenge is that 71% of people who die of cancer, die from cancers that have no screen. In fact, 45 out of the 50 cancers that GRAIL screens for have no screen today, like pancreatic cancer, for example. And so, there's no ability to catch it early.

And so, when GRAIL published their data at the end of 2019, we realized this was a huge breakthrough and that this would save a lot of lives. That's sort of how we initiated the process to acquire GRAIL. What we want to do is bring the GRAIL test to market as fast as possible to people around the U.S. and around the world. GRAIL has a terrific technology, and Illumina, we have the commercial presence in over 140 countries around the world. We have the teams that can work on reimbursement and regulatory approval, and so we can dramatically accelerate getting this test into the hands of people whose lives it could save.

SAFIAN: And so, the FTC's argument though, is that by bringing GRAIL back to being part of Illumina, that somehow there may be other efforts in this area that will be competitively disadvantaged. In other words, GRAIL will have an advantage over others who are doing research in this area. Do I understand that right?

DESOUZA: Yeah. So the FTC has, actually in the last 40 years, never been able to successfully challenge a vertical merger, so if a company is buying another company that's not in its space. What the FTC is saying is that, by us getting into this space, we will reduce innovation in the cancer screening space, and that we will have an incentive to raise prices of sequencing for other players.

Now, that's just fundamentally not correct because there are no other players. GRAIL is the only player in that space, and they launched their product a few weeks ago. In fact, there's nobody even developing a product like that. There are startups that have announced that they're working on single cancer blood tests for screens, or maybe up to eight to 10, but they're a while away from getting into the market, and nobody's done 50. And so, first of all, there's no competition in that market to foreclose on.

Secondly, they argue that competition may be chilled, and that's not at all been the experience. We have been delivering clinical tests since 2013, when we entered the non-invasive prenatal testing, NIPT, space and then a few years we entered the clinical space for therapy selection for cancer patients. And what we saw in both of those cases, and we'll start with NIPT, is that once we bought our way into that space, the number of players in that space went up to compete with our offering. A lot of them use our technology to compete with our test. The number of tests ordered by pregnant moms went up, the price to the consumer of the test went down, reimbursement went up, and

the sequencing price that we charged our competitors went down. So it was vastly pro-competitive and the same thing happened in the cancer therapy selection space.

Now, why is that? It's because the venture community tells us that once we enter a space, first of all, it validates the space to say, "Okay, this is real and it's happening." And then two, the work that Illumina does to put reimbursement in place, to establish regulatory pathways is work that every other company in this space can leverage. So once a billing code is established by CMS, that's a billing code that any of our competitors can use without necessarily having done any of the heavy lifting to get that code. So what we saw in both the NIPT space and in the cancer therapy selection space was that competition flourished.

We also have a very strong incentive at Illumina to make sure competition flourishes. In both NIPT and in cancer therapy selection, if you combine them, we make 10 times as much revenue selling sequencers to our competitors than we do from selling our own tests. So we have a powerful economic incentive to make sure there's a lot of competition because our core business is to sell the sequencers.

SAFIAN: I'm curious, did you expect that so much of your job as CEO, or a certain portion of it, was going to be dealing with the FTC on these different kinds of deals?

DESOUZA: I think everybody was surprised by the actions of the FTC on this deal. I think the prevailing wisdom and the economic experts tell us that this is not typical for the FTC to do. Again, they've not successfully challenged a vertical merger in 40 plus years and then the way it's playing out in Europe is also not typical. The European commission actually has no jurisdiction as a whole or in any of its 27 countries because GRAIL does no business in Europe and has no plans to do business in Europe for awhile. But the European Commission invoked article 22, which is something they've really never done before.

SAFIAN: I understand you were recently in DC meeting with congressmen and senators for the first time, what was that like?

DESOUZA: It was definitely a novel experience. We at Illumina, we're sort of an engineering science company, and so we don't spend much time in DC, but it's clear that there is a need to.

What I heard in DC were a few things. One, I think there was just almost a little bit of shock and awe that a test like this exists. One member of Congress who actually has a medical background, I think two minutes in, his first words were like, "Wow. This is doable?" And although the GRAIL test has been on the market now for a few weeks, they don't really have a substantial marketing department to get the word out, and so most people don't know the GRAIL test exists. There was a huge amount of pride that

this test was developed here in America and that it's two American companies we're talking about.

And then there was just, honestly, a lot of disbelief around how this process is playing out. They were confused about what is happening from a regulatory perspective. There's a huge amount of support for getting this test out as quickly as possible and to get this beyond the self-pay market where it is today. So today, because GRAIL doesn't really have the reimbursement in place or the teams that can drive it, the test is offered as a self-pay test. And if you go to their website, you'll see it costs $945 for the test. It's a life-saving test, but a lot of people can't afford, especially regularly, a $945 test.

What we don't want is this test withheld from communities that already are underserved from a healthcare perspective. And so there was a lot of interest in seeing how we can accelerate getting this test out to as many people as quickly as possible.

SAFIAN: You mentioned that the core part of your business is the sequencing machines, as in the sequencing process, as opposed to the testing, I'm curious whether this is a distraction for you. How important is GRAIL relative to other things that Illumina is doing?

DESOUZA: I'll start by saying that at Illumina, we are focused on improving human health by unlocking the power of the genome. So that's the mission we've been on for a very long time now. And our focus in doing that primarily is, as you said, to develop sequencers. So our sequencers today are used by children's hospitals to diagnose children that have genetic diseases, they're used by cancer hospitals to match cancer patients with the right therapies, they're used for carrier screening for people that are considering having a child, they're used in consumer genomics by companies like 23andMe, for example. But they're using a whole set of different fields, including as far a field as agriculture or even companies that are looking to store IT data in DNA. So there are hundreds of markets that we serve. We have 7,000 customers around the world, and in most cases, actually, we don't even know what they do until they publish their paper or launch their product because people just buy our sequences and do their thing.

Now in a small set of markets, we offer the test ourselves. So we do both, we have our own tests, and we enable players who compete with our tests. The reason we did that is because we felt we could accelerate those markets, and where we feel there's a big market and the presence of Illumina will accelerate the market, we get in.

Economically though, the vast majority of our revenue comes from sequencers. That's still the biggest driver of our revenue, our profits, and you see a lot of growth in that part of the market, too.

SAFIAN: Steve Jobs used to famously ... He'd worry about what the next thing was and wasn't worried about what the core business was. It was always the next product. For you as a leader

trying to scale this business and really scale the way genomics can change and affect human health, how do you balance those pieces of it?

> **DESOUZA:** I'm definitely spending a lot of time focusing on things that will impact us sort of in the three-plus year timeframe. In a lot of cases, we help accelerate the market in a particular direction by the investments we make in our technology. And so we spend a lot of time thinking about, "What products can we bring, in the markets that we're in, to accelerate it?" But also, "What work do we need to do from a reimbursement perspective or a regulatory perspective, a physician education perspective, so the doctors know to order those tests, to accelerate those markets?" And then we look at, "What are the breakthrough markets that are emerging?" And that's what led to the acquisition of Grail.

SAFIAN: Before the break, Francis DeSouza, the CEO of Illumina, was explaining how he got crossways with the FTC and why he feels the risk is worth the challenge. Now, we're going to dig into some lessons from Illumina's Covid-19 experience, which began at the outset, in Wuhan. The takeaway here is about making the most of an opportunity – whether planned or unexpected. By focusing on a long-term mission, DeSouza has been able to advance an emerging marketplace, even in the short-term.

And so over the last 18 months, there's been certainly discussion about the accelerated adoption of technology overall because of the pandemic, that it's been accelerated by five, 10 years. In that health science area, obviously with mRNA vaccines, that has accelerated or feels like it's accelerated. But in your core business, does it not accelerate faster because of sort of adoption and recognition of it? I mean, you have to move at the pace of science, or can you speed things up?

> **DESOUZA:** You can absolutely speed things up once you have a product, by working on things like reimbursement and regulatory pathways and education. A lot of times you have to educate the doctors on what the test is, when it can be used, and how it can be used. And so this is a market where bringing the product out is in some sense just the beginning of the journey.
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> Now, you brought up a really good point about the pandemic. I believe the pandemic has accelerated the field of genomics by five plus years. Our team was actually called into Wuhan at the end of 2019, and the first viral genome of SARS-CoV-2 that was published on Jan. 10 was done on Illumina sequencers out of Shanghai.
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> We, since then, have been involved not just in China, but around the world in doing surveillance of how this virus is evolving. So when you hear about the Delta and the other variants, a lot of that is done on Illumina sequencers. We've also donated sequencers to, and consumables to, over 10 countries in Africa. I know we were in Mozambique the other day training teams on the ground on how to use sequencing. And some of these countries have never had sequencing before. We were used in India to track how the variants are emerging there. And so we've seen this whole field of

genomic epidemiology emerge, and we've seen genomics enter sort of the vernacular of the culture, where people are talking about variants and mutations, and they're very aware of what genomics does.

We've seen other fields accelerate, too. The whole area of genomic vaccines, mRNA vaccines. We worked with Moderna and BioNTech. Moderna, their entire vaccine development program is based on the data that comes off Illumina machines. And mRNA vaccines for COVID are only the first step for them. They're working on cancer vaccines and malaria vaccines.

We've also seen acceleration in the use of liquid biopsies for cancer patients, and that's using blood tests instead of tissue samples. And so we saw a whole set of fields in medicine dramatically accelerated through the pandemic.

SAFIAN: And so this is in some ways, as you're describing this, this is sort of an adoption of science and technology that existed, but just wasn't applied to these purposes or with this breadth.

DESOUZA: That's exactly it. And we have been doing work now since the first human genome was sequenced in the beginning of this century, so two decades now. We've seen the emergence of gene therapies over the last 18 months to two years that are having really dramatic results with curing a patient of sickle cell cancer, or inherited blindness. We've seen the emergence of CRISPR and gene editing into the clinic in the last couple of years. So again, technology has been developed over the last couple of decades, whereas now finding clinical applications.

SAFIAN: Yeah. A lot of the listeners to this podcast are entrepreneurs and intrapreneurs, right? They're engaged in trying to figure out how to scale. And as I'm listening to you, there's this sort of balance, I guess, that I'm curious about, like what things you make happen to be able to generate that scale, to accelerate that scale, and what things are like you keeping your eyes open and saying, "Oh, here's something that I can delve into further. There's already momentum in an area that I can make more of."

DESOUZA: That's a great observation. There are things that have been developed over the last couple of decades that are now ready for prime time. But there are also a number of things that are really exciting that are much earlier stage, that are in the stage of when we first discovered GRAIL. Where you look at something and you think, "Wow, this could have a massive impact in the next five to 10 years." At Illumina, we spend about 18% of our revenue in R&D, which is twice our industry's average, and it's a statement partially to the opportunity in front of us that's just so vast, and we're still so early on.

SAFIAN: And I guess the more sequences that are out there, the more data that's being collected that you can then look for these patterns, that as you talk about GRAIL, you weren't necessarily looking for that pattern. It just sort of emerged from data that was being created.

DESOUZA: You're absolutely right. We weren't looking for it. We were looking to understand the health of the baby, and we stumbled upon signs of cancer in the blood in the mom. And that is going to continue to be true. The more data we collect, the more we'll understand how genomics and your genome translates into health and disease.

What's exciting, too, is that with the advances in machine learning and AI, you can actually find signals that are very powerful before you even understand the biology. And that's what happened here in cancer screening, where initially we thought you would be looking for known mutations in cancer genes. And so we said, "We know that these mutations in these genes give you a much higher chance of having cancer."

And we did those tests, but at the same time, we unleashed the AI algorithms to say, "And look for anything else, and see if there's any other signal that we don't understand, but may be better."

And what we found was the AI algorithm sort of developed very complex signatures based on methylation patterns that are very, very, very indicative that a person has cancer, and also point to where in your body the cancer is. In 93% of the cases, that blood test can tell you if you have a cancer, what tissue it's in. So, "It's in the pancreas." And frankly, we still have work to do to understand why. What's the biology that drives those incredibly complicated methylation signatures? Hugely exciting area of research. It also points to the opportunity for a new area for drug targets to say, "If those methylation signatures are deeply associated with cancers, then what if you could disrupt them?" And so to your point, the more data you have, the smarter we get, and the better our algorithms are that can help us lead the way.

SAFIAN: The last year, year and a half, and I've had this discussion with other folks in the medical science areas, such an opportunity in the midst of a really difficult year in so many ways. When you look back on the last year, year and a half, for Illumina, has it been a good year, has it been a bad year, or a hard year? How do you encapsulate what the experience is of going through this?

DESOUZA: It's been a hugely tragic year. When you think about the last 18 months, so many people have died, there's been so much suffering. This huge human cost, the stress of people being cooped up at home, the pressures of people losing their jobs, the pressure of people that lose their insurance, the enormous frustration of seeing the inequity of access to vaccines, the inequity of access to testing. And it's highlighted just really problematic structural issues about equity in our society here in the U.S. and around the world.

And in the midst of that, we've seen people rally and on the front lines, have done just heroic work. And part of that are the scientists. It has been just an unbelievable year in terms of medical innovation and scientific innovation. The mRNA vaccines are ... It's hard to use any other word other than miraculous. Vaccine development takes 10 to 15 years on average. The fastest for mumps was four years. And yet in less than a year, we went from identifying a pathogen to having a highly, highly effective vaccine for it. I got goosebumps, and I was choked up when I saw the first trucks starting to roll – I still get choked up when I think about it – starting to roll at the Pfizer vaccines that got published. It truly was just miraculous work that happened.

SAFIAN: I mentioned that there are scale leaders who are listening to this. Are there lessons about scale and otherwise you would draw from the experience you've had dealing with the acquisition side, dealing with the government? Are there things that maybe you would have done differently or that you would try to do differently next time you might warn people about?

DESOUZA: I think we did a number of things right, especially around innovation. But there are definitely areas I think we could have done better and I think we will work on to do better in the future. One is it turns out it is important to have a presence in DC. It turns out it is important to spend time making sure that the people that are driving policies and regulations really understand A, what's at stake, B, what the market actually looks like, and that's something that I wish we had done more off earlier and something we will start to do more of going forward.

SAFIAN: A lot of tech companies cite competition from China as evidence that whatever monopolies may seem like they're in place, the alternative is to cede ground to Chinese firms that are government connected. Is that similar for Illumina with the Beijing Genomics Institute?

DESOUZA: It is part of the discussion. Today, we at Illumina, and we at America, really are the leaders in genomic sequencing. And it's a field that we've been leading for a while and it's through big investments we make in R&D. BGI does sell sequencers around the world, we believe, and it's been validated in court that they are infringing on our IP, that they're using some of our technology. And it's going to continue to be a race, keep staying ahead of where the market is. If we are blocked from getting into other areas and BGI is not, it does create an uneven playing field where, to the point you made earlier, BGI will just have access to more data to drive more innovation than we will. And if we let that happen, then we risk losing our lead in this very, very important area for the future.

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

DESOUZA: The single biggest thing that's at stake is that we know if we acquire GRAIL, tens of thousands of lives will be saved that wouldn't be saved if we don't acquire GRAIL. That motivates us deeply. We feel there's a moral imperative we have to push as hard as we can to make sure that everybody understands that and that we do get this

test to everyone. We are deeply passionate about equity of access to genomic technologies. It's why we drive the cost of sequencing down so aggressively as we have, and we don't want to get into a world where genomic tests are only available to the self-pay market and the wealthy. And so that's the biggest thing at stake. There are tens of thousands of lives that we could be saving by accelerating the access to this test.

SAFIAN: Well, this has been great, Francis. I really appreciate it.

DESOUZA: Likewise, thank you.

SAFIAN: To share this episode with a friend, go to mastersofscale.com/rapidresponse.