[SQUEAKING]

[RUSTLING]

[CLICKING]

PROFESSOR: Today, we have a special guest lecturer, Professor Andrew Lo. A lot of you may have already known Professor Lo, but I still will make a quick introduction. So Professor Lo is professor at the MIT Sloan Business School for many years. He's also the director of the Laboratory for Financial Engineering and a principal investigator with MIT CSAIL, which is the Computer Science and Artificial Intelligence Lab.

He also has many other active involvement with, say, just a couple of examples. Santa Fe Institute and NBER, which is a National Bureau of Economic Research. And Professor Lo's research areas are very broad too. So I think it will be too long for me to read through them. I think instead of that, I will pass it on to Professor Lo for today's lecture.

ANDREW W. LO: All right. Great. Thanks very much, Jake. Thank you, Peter, for inviting me to 18.642. Happy to be here. And I'm going to be talking to you about some big ideas, and some big challenges, particularly for your generation, because our generation has created the problems that your generation is going to need to deal with.

And so what I'm hoping to do today is also to give you some of the tools by which you can deal with some of those problems, problems like climate change, like dealing with cancer, various kinds of energy demands that are growing exponentially even as we speak.

So by background, I'm a financial economist by training and trade. Got my PhD at Harvard in economics, financial economics. Then ended up teaching at the Wharton School. And for the last 35 years, I've been teaching at MIT at the Sloan School in the finance group. And when I teach my first-year MBAs in finance, I start off by telling them, finance is the most important subject you will ever take at a business school. And I acknowledge that my other colleagues in departments like accounting, and marketing, operations research, they may feel the same way about their subject.

But the key difference is that in my case, I happen to be right. And the reason is because no matter what you do, no matter what field you go into, no matter what industry you choose for your job, at some point or another, when you want to do something really important, really transformative, you will need money. And at that point, you will be speaking my language. You will need to understand the basics of financial analysis, things like cost of capital, net present value calculations, and so on.

So in this very short and compressed lecture, I'm going to give you an exposure to all of those concepts in the context of dealing with some of society's biggest issues. And I'm going to focus on two in particular. One is in biomedicine, and the other is going to be in energy, particularly fusion energy.

So let me first start with an observation on the first set of examples. And that is that biomedicine is at an inflection point. Now some of you who are biology majors, you know this. Actually, do we have any biology majors here in this class? Anybody doing anything in bioengineering? How about chemical engineering? Chemistry?

AUDIENCE: [INAUDIBLE]

ANDREW W. LO: OK. All right. Well, people do math and other subjects. But anyway, it turns out that in biomedicine, things are different than they've ever been in the history of the field. And I'm going to give you two examples of that.

The first example has to do with these two kids, Caroline and Cole Carper. They were born with a rare condition known as Leber's congenital amaurosis. It's a single-gene mutation, a typo in your DNA, that causes blindness starting at birth. You're born with a normal pair of eyes, but this mutation prevents your eyes from producing a very important protein. And without the protein, you start to go blind. So by the time you're six months old, you are legally blind from that point on.

And so these two kids were part of a clinical trial in 2016, started by a Philadelphia-based drug company called Spark Therapeutics, that used a really remarkable therapy to try to deal with their genetic mutation. It's a treatment known as gene therapy. And the way it works is this. You take the correct version of the gene that these two kids don't have. You insert it into a virus. And then you inject the virus into the back of the eyes of these two kids. One-time injection.

And what happens is the virus infects the cells, and picks the correct gene, and swaps it with the incorrect version in those cells. And from that point forward, these kids' cells in the back of their eyes start producing this protein. And let me tell you what Caroline said a few days after she received the injection.

"I went outside when it was snowing, and I was like, oh, I can see the snowflakes. It was really cool to actually see something that I've never seen in my life before." One-time injection, and now, she can see.

The second example has to do with a disease known as Canavan disease. So this is also a single-gene mutation, a typo. And what this disease does is pretty subtle. It prevents your nerve cells from being able to maintain the myelin sheath that basically provides the insulation for that nerve cell.

Now you all know that nerve cells have a nucleus, and they've got an axon, right, this long string that conducts electricity, and allows you to basically take an impulse and transmit it to various parts of your body. And the purpose of this myelin, myelin is a kind of fat. The purpose of this fatty sheath that goes on the outside of every nerve cell is insulation. It's like a wire that has to have some kind of insulation to prevent the electrical impulses to cross to other wires.

When that happens, you get short circuits. And obviously, that's a bad thing. Well, it turns out that kids with this single-gene mutation, after they're born, the myelin sheaths in their body begin to degrade. And so the electrical impulses start to short circuit. And so you have a hard time controlling your muscles.

And so generally, these kids have a lifespan of about 10 to 12 years. This is an example of a Canavan patient. He's probably close to his end of life. They generally don't grow beyond 15 just because it becomes harder and harder to control your breathing, your heartbeat. All of the bodily functions that we take for granted become much more difficult in Canavan patients. You'll notice that he's leaned back on his wheelchair. The reason is that his head tends to be larger than normal. This hyperencephaly, your head gets bigger, is part of the symptom of the disease.

And at some point, your neck, because there's no muscle tone, because you can't use the muscles because of the nerve impulses that get short circuited, it's very easy to snap the neck if you just lean over like this. And so you have to always be in a prone position, and your head protected by these cushions.

There's lots of other terrible symptoms. Let me tell you what they are. Children with Canavan disease cannot crawl, cannot walk, cannot sit, or talk. Over time, they may suffer seizures, become paralyzed, developmentally delayed, blind, and have trouble swallowing. Deafness may also result. Many children do not live past the age of 10. And at present time, there is no cure for Canavan disease. Treatment involves managing the symptoms.

And so the typical Canavan patient, the disease generally affects you starting at birth. But in some cases, it can get progressively worse over time. The doctors that know how to diagnose this disease, typically what they tell their parents is, go home and love your child. That's their treatment. That's it. That's all they can do.

So it turns out that you can treat this disease using the same technique, gene therapy. Take the correct version of the gene, put it into a virus, inject the virus, in this case, into the brains of these Canavan patients. And well, I'm going to show you a video clip of what happens with one particular patient. This is patient number three, I believe. And what you're going to see is a clinical trial of the patient before the treatment, after she's diagnosed. So they know that she's got this mutation. You can see the symptoms that are developing.

And the frustrating thing is that you are born relatively normal. But because your body can't maintain the myelin sheaths, you begin to degenerate over a period of time. So let me show you what's going on here. So this is June 2022 just before the treatment.

[VIDEO PLAYBACK]

- So this is the patient.

- You eating your blueberries?

- And she's about one year old. And so at this age, you should be able to move around. But look at her hand motions, and how jerky her control is. It's going to take her quite a while just to grab one blueberry and put it in her mouth. So this is going to get much, much worse at this particular rate of degeneration.

[END PLAYBACK]

[VIDEO PLAYBACK]

- Now this is about six months after that one-time injection.

- Wow. Look at you trucking along. Come on.

- She's actually walking, even though it's with a walker. She's actually able to walk. Now you can tell that there's still slow--

[INTERPOSING VOICES]

- She can't walk on her own yet. But this is only six months after the treatment. OK? Now this is just around the same time. She is now getting ready to actually stand on her own. And this uses an enormous amount of core muscles. You probably all know you have to exercise your core. So she's developing core muscle strength. She can't quite do it yet, but she's close. Very close. And--

- There you go.

- There she goes. She's just about to do it. That's it. For the very first time, she actually stood up on her own. Amazing. Now this is a month after that. She is walking without the walker. She can't do it all on her own yet, because remember, it's only been about seven or eight months since her body is able to deal with this myelin sheath problem. But way better.

Now this is about nine months later. She's on a bike, which is extraordinary. And she's motioning to her dad to give her a push, and to help her out. And here she is just a few months ago this year. So this is now about a year and three months after that dose of gene therapy. She's about to be able to walk on her own for the very first time.

There has been no Canavan patient in the history of the disease that has ever been able to do this. And so this is remarkable, remarkable progress.

- Can you blow me a kiss?

[KISS SOUND]

Thank you, honey.

- She is actually reading now. She's starting to learn the letters of the alphabet, and she's responsive. She can actually interact. This is extraordinary.

[END PLAYBACK]

ANDREW W. LO: The blind shall see. The lame shall walk. That's a phrase that we usually associate with religious experiences. But it's happening. It's happening now thanks to the miracles that are being developed by these scientists and clinicians. And our colleagues, Phil Sharpe, Susan Hockfield, and Tyler Jacks, they published a paper in 2016 to describe this new world that we're living in. They call it, convergence. The convergence of the life sciences, physical sciences, and engineering, all of these fields are coming together to be able to do things that people were not able to do before.

The other term that people in biomedicine use is the omics revolution. All of these omics have experienced tremendous progress over the last even five years, never mind 10 or 20. And genomics, the science of sequencing your genes, epigenomics, the on-off switches that cause certain genes to be switched on, and others to be switched off, transcriptomics, the various different ways that you can turn sequences of genes into proteins that are in your body, proteomics the 20,000 to 25,000 proteins that are being produced every day by your body.

Metabolomics, the chemical reactions that make life possible. And finally, most recently, microbiomics, the colonies of bacteria that inhabit our bodies that keep us healthy.

All of these omics have given us tremendous new knowledge based upon research that's been going on thanks to convergence, with the exception of one. There is one omics that's been the bottleneck to progress. And you know what that omics is? Economics. Because you got to pay for stuff. And we're using the same old stuff, the same old business models, to try to do those kinds of financings. So what I want to tell you about is a challenge that economics is facing, and how we can get around that challenge.

And the challenge is this, the valley of death. When I first started getting interested in health care, I would talk to scientists, and doctors in Boston, Cambridge. We have a lot of them, as you know, very, very good ones. And I would ask them, why isn't there more progress? And it keeps telling me about the valley of death, the valley of death.

So I'm thinking, what does southern California have to do with progress in biomedicine? And then they tell me, no, no, no. It's not a place. It's actually a metaphysical concept of the period between scientific experiments at university and medical centers, and first in human clinical trials. That period in between those two milestones is the valley of death, meaning that it's really hard to raise money to fund those kinds of things.

And so money is something that I've spent a lot of time studying. So my initial reaction was, why? Why is it the case that there is a valley of death? I just assumed that if there was a patient in need, and there was some technology that could help that patient, that magically, money would appear to fund the drug or a device, and everything would be hunky dory.

Turns out that that's not really how the world works. And the more I studied the problem, the more I realized that actually, the valley of death exists not just in health care, but in many fields because of increasing risk and uncertainty. Now what do I mean by risk and uncertainty? I think you all know what risk is. Risk is the kind of randomness that we can parameterize. So normal distribution, gamma distribution, chi squared. We can figure out the probability laws of risky things.

But the uncertain things, those are what economists refer to as the unknown unknowns, because nobody's ever done them before. There's no data. So you can't assess the probability that this could possibly happen. And so that's the challenge that the valley of death ultimately needs to overcome.

Because drug development is a very lengthy process, as some of you may know, you have to go through clinical testing. And because of that process, there are three things about investing in drug development that investors have to get their arms around. One, it costs a large amount of money to do the testing, hundreds of millions to billions of dollars, in order to get one drug approved.

Second, that process is generally very, very unlikely to succeed. Low probabilities of success. And third, it turns out that developing a drug can take 10 to 15 years from beginning to end. So if you compare that with developing an app, how many of you have actually developed an app already? Yeah, so I imagine that it doesn't take you $100 million to do that. And it doesn't take you 10 or 15 years. And it doesn't take you a whole team of people, where you're going to fail with a probability of whatever, 95%.

So that's the problem with investing in this. And so I'm going to give you an example of why this is so challenging by asking you to think about investing. Some of you may already have invested, especially given that we're at MIT. I often encounter undergraduates who are actually quite accomplished traders and portfolio managers.

But let me give you the example that I give my first-year MBA students, and see how you do with this. I show them four different financial investments. I don't tell them what they are, or even over what time period they span. I just tell them, this is what happens when you put a dollar into it, and you leave it there for an unspecified, multi-year investment horizon.

The green line turns a dollar into $2.00. Not very rewarding, but not particularly risky. The red line turns $1.00 into $5.00, way more rewarding, but way more volatile, lots of ups and downs. The blue line turns a dollar into about $8.00, the most rewarding of all, but also the most volatile. And the black line, somewhere in the middle. Not the most rewarding, but relatively reasonable amount of risk.

So if you could have only one of these investments, you can't mix and match them, if you only can have one to put your life savings, or better yet, to invest your grandparents' retirement money, and you had to do it for them, they asked you to help them, which would you pick? How many of you would pick the green line to invest? Wow, no takers?

OK, how about the red line? How many people would take the red line? No takers for the red line? I want you to remember this moment, because I think some of you may want to call your brokers afterwards when I tell you what the red line is. How about the blue line? How many people want to do the blue line? OK, we got one or two entrepreneurs in here, or hedge fund manager. OK good. And then now the black line. How about the black line? Yeah, by far the most popular choice in my MBA class as well. And when I ask them why, they say, well, it's got the best trade off between risk and reward. Yeah, question.

AUDIENCE: Isn't the black line [INAUDIBLE] Ponzi scheme?

ANDREW W. LO: Really? I don't know. Let's see. First of all, let me tell you what the four assets are. And we'll talk about that. The four assets are the green line, treasury bills, safest asset in the world, at least for the next few weeks. We'll see whether the budget discussions go well. As long as we agree to pay back our debts, yes, safe asset. But you know what? You put your money in it in 2008, you would have earned pretty much nothing. And actually, you would have earned less than nothing because of inflation if you look at the real return.

All right. The red line that none of you picked, that is the US stock market. I bet you some of you may already have an investment in the S&P 500. Right? But if you didn't pick it, or if you did pick it in 2008, congratulations. You would have done just fine since then. Very, very good return.

The blue line that only one of two of you picked, that is the single pharmaceutical company, Pfizer, one of the largest pharma companies in the world. And if you had picked Pfizer in 2008, well, double congratulations. You would have done spectacularly well since then. Lots of volatility, but really quite well.

Now the black line, that is the returns to a fund called the Fairfield Sentry Fund, which most of you have probably never heard of. But that was the feeder fund for the Bernie Madoff Ponzi scheme. So quite right. You got the correct answer. I had to stop it in 2008 because the Ponzi scheme ended up blowing up then.

Now I show this example to students because I want to explain to them something very common about human nature. And that is that we all, as investors, we want high yielding, low-risk assets. And we have a name in finance that describes it. It's called the Sharpe ratio, after Bill Sharpe, the Nobel-Prize-winning economist from Stanford, who pointed out that people care about the expected return of an investment above T-bills per unit of risk that they're taking. They want to have the highest expected return per unit risk. High Sharpe ratios.

So what's the Sharpe ratio of these investments? Well, it's 0.33 for the S&P, point-- sorry, 0.34 for Pfizer, 0.33 for the S&P. And on paper, the Ponzi scheme had a Sharpe ratio an order of magnitude higher. And that's how Bernie Madoff suckered all of these poor investors to put money with him. $50 billion of investor money that he essentially stole because of this common fact.

Now it turns out that biomedicine has had a Sharpe ratio that's been declining over the last several decades not because the numerator is unattractive. There are many biotech companies that just do super well. But the problem is the numerator. The numerator is growing even faster. The risk, as well as the uncertainty is growing as we become more sophisticated about the science and medicine of disease.

And so we need to figure out how to increase the Sharpe ratio. That's the goal. So I know this is a math class. So I could not possibly do a presentation here without giving you at least one equation. So I'm going to give you an equation. And it's going to be a very difficult math challenge about how you can increase the Sharpe ratio.

It turns out there are two ways of increasing the Sharpe ratio. And let me tell you, for those of you who aren't as mathematically gifted as I am, you can increase the numerator, or you can decrease the denominator. Those are the two ways. Now of course, in my MBA class, I have to have a student who raises his hand and says, Professor Lo, there's actually a third way. And I said, oh, really? He said, yes, you can do both. So yes, I agree. You can do both.

It turns out that we are doing both. Better science, better engineering, better organizational structures, on and on. All of those are designed to increase the numerator and decrease the denominator. But the one set of techniques that have not been used as much in biomedicine as well as in other industries that I'm about to tell you is new financing and business models. And that's the interesting opportunity for mathematicians, believe it or not.

There are ways of constructing new business models using math that could actually change the risk-reward trade offs of these investments. So let me show you. I'll give you an example.

Suppose I give you an opportunity to invest in a new fund that I'm creating. I need $200 million to launch my fund. And I'm going to be investing in all sorts of special technologies that only I have access to. You don't, So it's proprietary. It's going to take me 10 years before I give you any payoff whatsoever. So don't bother asking me before the decade is out whether or not I'm going to give you anything back. It's going to take at least that long.

And in full disclosure, the likelihood that I give you anything back is 5%. 95% of the time, I'm not going to be able to produce anything after 10 years. OK? How many of you would invest with me?

AUDIENCE: Depends on the return.

ANDREW W. LO: Thank you. Most of you didn't even bother raising your hand. But you, you want to know what the return is. Fair enough. That's absolutely right. For most of my MBA students, they don't bother asking. When they hear $200 million, wait 10 years, 95% failure rate? No thank you. Not interested. But I will get one or two MBA students who will ask, what's the return? So let me tell you.

These are the back-of-the-envelope calculations for what a single anti-cancer drug will do in terms of potential revenues and success rates. It takes about $200 million to do the clinical trials. It takes about 10 years to do them. And in oncology, the historical success rate is actually a little less than 5%. 3.4%. But I'm going to use 5% as round numbers.

If you are successful, though, in the case of cancer drugs, you will get $2 billion of revenues from years 11 to 20. Why 11 to 20? Well, because it takes 10 years to develop a cancer drug. So if you're successful, then starting in year 11 is when you begin to generate cash flows. And why until year 20? It's because that's how long a patent lasts. After year 20, your patent is gone. And people can compete with you, and your profits go way down.

Two billion, two billion, two billion from years 11 to 20. That is equivalent to a single payday of $12.3 billion in year 10. OK, so now let me ask you the question one more time. I need $200 million up front. Wait 10 years. 95% of the time, I'll give you nothing, maybe a warm handshake and goodbye. And 5% of the time, I'll give you a check for $12.3 billion in year 10. How many of you would invest in that?

AUDIENCE: It would depend on [INAUDIBLE].

ANDREW W. LO: No. No. I'll take whatever--

AUDIENCE: [INAUDIBLE]

ANDREW W. LO: Whatever money you have. How many of you? All right. I'm getting one or two hands, but not a lot. You're not all interested, because for most of you, it was way too risky. It takes too long, probability of success is too low, and it's just not your cup of tea. And sure enough, if we calculate the rate of return, this is an expected rate of return over this 10-year period of about 12% with the standard deviation of 423.5% for a Sharpe ratio of close to 0. Nobody's interested in this, or very few people.

So this is where financial engineering can make a difference, and where math comes into play. A very, very small amount of math. Instead of investing in one of these drugs, why not invest in, oh, I don't know, 150 of them all at the same time?

If we did that, if we invested 150, you might say, well, wait a minute. That takes 150 times 200 million, which is $30 billion. That's not the kind of math that would make anybody excited. $30 billion. Where are you going to get $30 billion? And as an economist, I have a very simple answer for that. The answer is, assume we have $30 billion. I'll come back to this in a minute.

But if we had $30 billion, and if we assume that the 150 projects are statistically independent and identically distributed, and I'll come back to that assumption later, if that's the case, then the expected rate of return for the portfolio is the same because they're identical projects. But the risk now goes down by the square root of the number of projects. Why? Because the variance of the sum is the sum of the variances when they're IID.

And so if the variance is the sum of the individual variances, take the square root of that to get the standard deviation. That's why it goes down by the rate of the square root of 150, which gives you a 34.6% risk rate.

Now if I calculate the Sharpe ratio of this, I'm getting a Sharpe ratio that is an order of magnitude higher. How many of you would invest in this fund? Show of hands. I'm getting a lot more hands. That's where I'm going to get the money. I don't have 30 billion, but you do in the aggregate.

If I can make this investment attractive enough to get you to put some of your 401(k) money, or some of your summer internship money, into a fund like this, I can raise $30 billion very, very quickly. Now the question is, can you really raise $30 billion? And the answer, of course, is it depends. It depends on these calculations that I just did. It depends on the math underlying this portfolio.

The mathematics will tell you whether or not this is feasible. So I'll give you an example, where not only should it work, but it actually does work. And the example has to do with rare diseases.

So I gave you two examples of rare diseases at the beginning, Canavan disease, and Leber's congenital amaurosis. Turns out, there are roughly 12,000 different rare diseases. And so individually, a rare disease may have a small patient population like cystic fibrosis, hemophilia, Lou Gehrig's disease, or a number of other diseases. But in aggregate, there are more than 30 million Americans that are suffering from one of these 12,000 diseases.

I suspect that somebody in this room knows a friend or a family that's suffering from a rare disease. Anybody? Just show of hands. Do you? Yeah. So it is clear that it may be rare for any individual, but it is not rare over a population, because of just the number of mutations that are out there.

And so for a lot of reasons, it's actually relatively easier to develop a drug for a rare disease, both because typically, we know what's wrong. There's a very serious problem. And you can trace the origins to one particular organ, and within that organ, to one particular mechanism, and to that mechanism, one particular gene. So you know a lot about it. But the other reason it's often more successful to develop these therapeutics is because it doesn't cost as much money because it's a rare population.

So when you run the clinical trials, you can run them with a smaller number of people and still be able to demonstrate that the drug works, like the case for Spark Therapeutics.

In the case of that Leber's congenital amaurosis, I think they got an FDA approval with something like 30 or 40 patients. That's it, 30 or 40 patients in the clinical trial. And when they were able to restore their sight, the FDA said, you don't need to do any more testing. We're ready to prove it. This is an amazing drug.

But the key component is the fact that because these rare diseases are so different from each other, there's very little correlation in the successes and failures of different therapeutic programs. So when you calculate the variance of the sum, it really is the sum of the variances. If we don't have correlation, then can anybody tell me what the formula is for the variance of a sum of random variables?

AUDIENCE: Sum of the variance?

ANDREW W. LO: Sum of the variance.

AUDIENCE: It's covariance.

ANDREW W. LO: Exactly. How many covariances?

AUDIENCE: [INAUDIBLE]

ANDREW W. LO: A lot of them. Exactly. Because you've got A versus B, A versus C, A versus D, B versus C, B-- all the combinations. And so it turns out that when there's correlation, it's almost always positive. And so when you calculate the variance of a sum of a portfolio of typical investments, you're getting not just the individual variances, but all the pairwise covariances. If there aren't any pairwise covariances, that's where the risk reduction comes from.

And so rare diseases have this really cool property that I have to admit, I'm quite proud. I was the one who wrote a paper that recognized it. Frankly, I didn't think it was that big a deal except for this particular application. But it turns out that in the biomedical field, nobody had ever thought about this. The fact that because the diseases were so different, you ought to develop them not separately, but together in a single portfolio to get the risk reduction.

So instead of $30 billion, you only need 400 to 500 million. Instead of 150 projects, you only need 10 or 20 to get diversification. And so what did I do with this information? I wrote a paper. That's what we do in academia. Published a paper, ran a Monte Carlo simulation to show that if you actually used relevant industry numbers, the kind of rate of return you're looking at is around 22% per year. And with the volatility, that could be quite a bit lower than that, meaning a Sharpe ratio greater than 1.

Now you can ask Jake afterwards about whether or not a Sharpe ratio greater than 1 is good. As a professional investor and a risk manager for A Harvard management company, he can attest to the fact that this is a very attractive and very rare kind of opportunity. But remember, there are 12,000 rare diseases. So it doesn't seem that rare to me.

So the question is, does this really work? And the reason I wrote the paper was because I wanted people to try it out. And I got a phone call shortly after the paper came out from a former student of mine. Somebody who was a PhD in chemical engineering here at MIT took one of my courses when he was here, then went on, and became a biotech VC, and called me up, said, Professor Lo, I read your paper. Really interesting.

Would you mind rerunning your simulations, not with your assumptions, but with mine? And I said to this former student, of course. I'd be happy to. You know a lot more about the industry than I do. I'm just using industry averages, whereas you actually have hard data based upon your own portfolio investments.

So we ran a model with his parameters instead of mine. And the results, they look better. And so then I suggested a few other tweaks based upon what he was telling me about the industry, the way it works in his field. And we ran my version, and it looked better still. Over six months, I think we ran 35 different versions of this model.

And at the end of that six-month period, he came into my office and said, I just wanted to let you know, I quit my job yesterday. I'm going to do this. I'm going to build this company. And I got to tell you, that scared the hell out of me. I had never had that effect on any of my students. And he had a young kid in his household. And I said, Neil, you sure you want to do this? Maybe you should let me run a few more simulations. And he said, no, no, no. My wife is cool. I think we're ready to do this.

I felt guilty enough that I invested a small amount in the friends-and-family round. And in retrospect, I wish I would have invested a lot more because that's probably my single most profitable investment. In 2017, this company, BridgeBio Pharma, came out of stealth mode. And we had our first investor was not a venture capitalist, but a private equity firm that prior to this company had never invested in biotech. The company is called KKR. You may have heard of them. Some of you undoubtedly will be doing internships with them sometime in the next few years.

We raised about $40 million in that very first round after the friends-and-family round. A year later, we raised another 135, a year later, yet another 300. So we were right around the $400 to $500 million range. We had about 15 projects, just like the simulations. And at that point, we did an IPO, and after the IPO, we raised another 750. And as of this morning, or early this morning, before the market opened, BridgeBio is currently trading at about $4.6 billion of market cap.

All of the investors, myself included, have done better than we ever would have expected, a great rate of return. But you know what? That's not what this company is proud of. What they are most proud of is the fact that there are other portfolio companies that have gotten started, thanks to us. And it's now become a thing that you can use portfolio theory to reduce your risk, as this McKinsey report in 2021 put out. And at this point, BridgeBio has about 20 different projects in the clinic. Two drugs have already been approved.

In 2021, a drug focusing on a very rare kind of enzyme deficiency, as well as a rare kind of bile duct cancer. Both of them were approved in 2021. A third blockbuster drug looks like it's going to get approved sometime later this month.

So watch the news for an announcement from BridgeBio. And that gene therapy for that little girl who had Canavan disease, that turns out to be a BridgeBio drug. And as of last year, that drug with 10 patients have shown efficacy in every single one of the patients that have the disease. So we expect that the FDA will approve that drug sometime next year. Really amazing. And I got to tell you, the proudest professional accomplishment that I've ever experienced was this moment here when I met that little girl.

She actually lives in Boston in Jamaica Plain. And here she was. The parents found out about the business model that I had developed along with Neil, and asked to meet with me. And it was really kind of a scary and extremely emotional meeting. This is the Flour Bakery right across the Salt and Pepper Bridge, where Mass General is. That's where they were going for their care.

And I went into this Flour Bakery to meet them. And my first vision was walking up the stairs holding her father's hand. And she kept pushing his hand away because she wanted to do it on her own. It's just an extraordinary, extraordinary moment. This is the power of financial engineering. And let me be very clear. I had zero to do with any of the scientific decisions that BridgeBio made. I often tell people that finance cannot turn a bad drug into a good one.

But the lack of financing, or the wrong kind of financing, can easily take a good drug, and destroy it, and make sure it never reaches a patient. And so finance is an important aspect of drug development, but it is not the most important aspect. You've got to start with the science, and then figure out what the right financing is.

So I'm going to turn to my second topic now, which is energy transition. I want to illustrate the fact that finance is not just about biotech, but it really can transform any industry. And I know a number of you are concerned about climate change. So am I. So is Jake and Peter. And the question is, what do we do about it? Now there is this thing called energy transition.

And there's a report that I read a couple of years ago that I highly recommend. It's a rather harsh dose of reality. People talk about energy transition like we're going to get off of fossil fuels soon. And what this paper argues is that that's really not the right term. We are not taking less and less of our energy from fossil fuels. And here's a graph that illustrates it. So this is a graph of how much energy we are consuming as broken down by different sources.

So here. Oil, you can see certainly natural gas, and coal, all three forms of fossil fuels are growing in the amount that we're consuming year after year. Now how can that be? Because we are making progress with renewables. Right?

So here's wind and solar. This is in blue. And here is nuclear here. They're getting a little bit wider, but not nearly as fast as the fossil fuels are. And it's because human population is growing. And also, the kind of people that we have on this planet, that's changing. We are now having more and more people that are moving into the middle class. And when you move into the middle class, what do you want? You want a better life. You want a house, you want two cars instead of one, you want to take a vacation by flying somewhere.

All of the things that you and I take for granted, there are millions to hundreds of millions of people that are for the first time, being able to experience it. And that's why the consumption of energy is growing far faster than our ability to create non-greenhouse-gas sources of energy. So the problem with energy transition is that if you just look at what's going on, we can't just rely on renewable energy. We need to have low-carbon forms of energy that don't pollute the atmosphere, and that are on demand, available.

So what are we doing? How are we transitioning from one energy source to another? It's not really transitioning. We're not declining our usage of these kinds of sources of energy, but we need to be adding to them with low-carbon sources. And so from what my experts in energy, my colleagues here in the geo department are telling me, they're telling me that there are three sources of energy that is non-renewable. They're not wind and solar, but they are ultimately going to be infinite, close-to-infinite, sources of energy. And that is fusion, fission, and geothermal.

And for a variety of reasons, we're not going to see a lot of progress in the near term for fission. We already have nuclear power plants. But the problem from a political point of view is nobody wants to have them near where they live. And nobody wants to deal with the mess of the fuels that ultimately, when they degrade, become radioactive and dangerous. So because the prices of fossil fuels are highly path dependent, this energy transition is very, very difficult to predict. And what that tells us is we need to start thinking about alternative sources of energy that are going to be sustainable.

And so it turns out that nuclear energy is the main source of sustainable energy for the long-term future of the human species. And there are only two forms of nuclear energy, fusion and fission. So as you probably know, fusion is when we split an atom, and you get more energy out than you put in. But fusion energy is where you squeeze atoms together. And it turns out that the squeezing gives you a lot more energy than the splitting of an atom.

It also turns out that fusion energy is the most abundant form of energy in the entire universe. Why? Because this is what powers stars, and that's where we get all of our energy other than geothermal. It's basically we're getting energy from the sun.

So fusion, turns out, can produce roughly 4 times more energy per kilogram of fuel than fission. And here's the kicker it does not produce long-lasting radioactive waste. When you are finished using fission-based energy systems like uranium, plutonium, you will have radioactive waste that in some cases have a half life of 100,000 years, which is a lot longer than I plan to live. So that's the problem. Whereas with fusion energy, it produces water, and helium, and maybe some tritium, which is radioactive. But it doesn't last that long.

And moreover, tritium is something that we need as part of our fusion inputs. So the problem with fusion is you need three things to happen, the so-called Lawson triple product. You need to take a compound, some matter, and you need to squeeze it together really hard because that's how you're going to get atoms to fuse.

Unfortunately, just squeezing it is not enough on this planet. You have to loosen them up so that they will come together. And that means you have to heat it to a very, very high temperature. And then you have to hold on to it for a long enough period of time so that the fusion reactions can happen.

So these are the three things that have to happen, temperature, pressure, and time. Now it turns out that on the sun, or in the sun, this happens relatively easily. The pressure gets created by gravitational pull. And the temperature increases as a function of how it pulls in through the gravity, the different combustible items. And as we know, once you ignite fusion, it lasts, and lasts, and lasts for many, many hundreds of thousands to millions of years.

So something pretty amazing happened here in Cambridge on Labor Day weekend, 2021. What happened is that MIT, in collaboration with a spin off that it created called Commonwealth Fusion Systems, they created a magnetic field that was so strong, that it will, in principle, be able to contain fusion reactions to the degree that we need in order to achieve ignition. It can actually light this plasma. And this demonstration occurred about five blocks from here on Albany Street.

They created a 20-tesla magnet. 20-tesla magnet. That is an extremely strong magnetic field. And the interesting thing about what happened here is that three months later-- and by the way, this is yours truly. I was there for this event. I collaborated with Dennis Whyte, the head of the Plasma Science and Fusion Center. So he kindly invited me to be there. This was, by the way, Sunday morning at 7:30 AM Labor Day weekend. I was out on the Cape with my family. And I abandoned them to come here. That's how nerdy I was. But it was an extraordinary historical event.

What happened after that, of course, was we saw that the Lawrence Livermore Laboratory, Berkeley, they actually created a truly exothermic fusion reaction, meaning more power came out than money went than energy went in, which basically says you're creating money out of nothing. If money is energy, then you're putting more money-- you're getting more money out than you're putting in.

Also, the regulatory authorities have agreed that fusion should not be regulated the way that fission is, which is pretty big. And yet another repeat of fusion in 2023. So the question that my colleague in the Plasma Science and Fusion Center, Dennis Whyte, and I have asked is, can we use finance to fund fusion? So we wrote a paper about this too.

And in this paper, we do a calculation that shows, yes, there is a path of creating a portfolio in order to fund fusion. Now a portfolio of what? So I have to answer that question. In order for me to answer a question about portfolio of what, I have to describe, what do I mean by saying, fusion? What do we mean by fusion? What I mean is to create a commercially-viable power plant, a reactor, that will generate enough heat to create a turbine that will spin and generate electrons to be put on the power grid. That's what I call, fusion.

And so what that means is you need this. You need a fusion reactor that will do its thing and generate heat. The heat will basically heat up water, water will turn to steam. That will basically cause turbines to spin. As the turbines spin, you generate electricity, and the electricity goes on existing power grids.

So this whole thing is what I'm calling, fusion. That's what I want to do. That's what I want to invest in. Now how do we do that? How do we invest in fusion? And the answer has to do with what it takes to achieve fusion electrons on the grid. These are all the components that experts tell me are needed in order to get fusion to happen. And so the question is, how do we do that?

And the answer, like anything else, is break it apart, look at it one by one, and figure out what you need in order to achieve these different components. So one of the things we need is sustained high-temperature plasma. So plasma is a fourth state of matter. When you heat something up to a certain temperature, it becomes plasma. The problem is as it gets hotter, it's harder and harder to contain this kind of matter.

And so you need to have some way to hold on to it. Well, magnetic bottles are what we're considering in one form of fusion. But if that's the issue of creating high-temperature plasma, then let's take it and break it apart. What do we need just to do that? And by the way, just to let you know what high temperature means, we're talking about 100 million degrees. 100 million degrees. That's hot. So how do we achieve that?

Well, it turns out that there are a bunch of things you need in order to do it. So what do we do? This is the portfolio I'm talking about. I'm talking about creating a portfolio of technology that, when combined, will allow you to achieve fusion. But even if never combined, they have value in and of itself. For example, advanced vacuum systems. It turns out that in order to achieve really high temperatures, you have to have ultra-pure conditions with no contaminants and no air, in particular. You need to have a vacuum system that works far better than your typical Hoover vacuum cleaner.

It turns out that if you can create that vacuum system, it has applications in many other things, like for example, in drug development. And so if you think about fusion not as one thing, but as a portfolio of a whole bunch of different technologies that have value in and of themselves, but that when combined, will have value for fusion, you can basically break it apart and do the kind of financial analysis that we just did with a single drug development project, and then put them into a portfolio, maybe 150 of them, and figure out the risk and reward, and be able to finance it.

So the idea is to create a multibillion dollar fusion mega fund, just like we did with the cancer mega fund, and finance all these different technologies. And imagine creating an incredible board of advisors. On the scientific side, you've got people like Mike Campbell, University of Rochester expert in laser technology, Steve Chu, former energy secretary, Nobel Prize winner, Rob Goldston, Dave Larbalestier, Ernest Moniz, also another former Energy Secretary that was an MIT faculty member, Dennis Whyte, the former head of the Plasma Science and Fusion Center, and so on.

And then on the business side, you've got people like Sam Altman, Jeff Bezos, Peter Diamandis, Bill Gates, Vinod Khosla, so on, and so forth, people that can actually help us manage the business models.

Now you might say, well, wait a minute. How are you going to get these people to be part of this effort? And that's a challenge, because the folks in blue, they're not motivated by money. So if I call them up and ask them to be part of this, I would doubt that they would even return my phone calls. They've never heard of me.

The folks in green, they have all the money. And so I'm pretty sure that, and actually I know a number of them already. So that's why I know that if I call them, they will not return my phone calls. But if you raise multi-billion dollars to deploy capital, all of them will return your phone call, not just because of the money. As I said, the people in blue, they don't care about money. And the people in green, they have all the money. They don't need your money.

But if you can actually show that there's a business path that allows you to achieve your goal of ignition, they'll all want to be part of it. And finally, how many of you, if I created a fund like this with these people, how many of you would put as a one-time investment, just one-time investment, $1,500 of your 401(k) money that you may have saved up after a summer internship or after your first year working at your job?

How many of you would put 1,500 into a fusion fund? That's where I'm going to get the multi-billions of dollars, because with 130 million households out there, if 3% of you put in $1,500, that's more than $30 billion right there. We can do this. This can actually be done. So there are many other examples of this. Yeah. Question.

AUDIENCE: Wouldn't the portfolio for the fusion of all those different things, wouldn't they be highly correlated these different industries as opposed to the drugs [INAUDIBLE]?

ANDREW W. LO: Well, that's a great question. Let's go back and take a look at it. So it's true that the entire fusion reactors of many different companies will be correlated. But they will not be perfectly correlated if they're using different ways of achieving fusion. One uses magnetic, the other one uses inertial. And so there are different technologies. But more importantly, if I look at this portfolio of technologies, so one of them is plasma heating systems, how to make things really hot.

The second one is advanced vacuum systems, how to keep things really clean and pure. A third one is magnetic confinement technologies, so how do you shape the magnets in order to keep the bottle from becoming unstable. Each of those things have nothing to do with each other.

AUDIENCE: Oh, right. OK. I thought they might. That's all. OK, that makes sense now.

ANDREW W. LO: Yeah, the technology, some of them do. But most of them do not. And that's where you're going to get the diversification. You're right. So lots of other technologies. The key to all of these are that they are long shots. Very, very low probability, or unknown probability, of success. They cost a lot of money, they take a lot of time, but the returns to society are huge.

And so that's why you need to have innovative financing for these long shots. The key to all of this is to have the right narrative, the right story to tell investors, about how you're going to give them a return on their investment. And that requires the right business models to be able to do that.

So I'm going to wrap up with a story that I use lots of times, because when I first heard it, I was so impressed that I decided that that was going to be my motivation for doing what I'm doing.

It has to do with this man, Professor Harvey Lodish. He's a biology faculty member here at MIT in the Whitehead Institute. Harvey, when he was an assistant professor in 1983, he was approached by a businessman asking whether he would collaborate with him to create a treatment for a rare disease called Gaucher's syndrome.

This is also one of these genetic typos, which prevents your body from producing important housekeeping enzymes. And without this enzyme, fatty acids build up in your spleen, your bone marrow. And by the time you're a teenager, if you have a very serious version of this disease, you're dead.

And so Harvey and his colleagues, they developed the treatment to deal with this disease by replacing the enzyme with an artificially-developed version of it. And this little company in 1991 got a drug called Ceredase approved by the FDA, the first-ever enzyme replacement therapy. They would just put back into these individuals' bodies the missing enzyme that their bodies don't produce. They can produce it outside, and give it to them.

And you may have heard of Harvey's little company. It's called Genzyme. And in 2014, Genzyme was purchased by Sanofi for $20 billion. Now that's not why I want to be Harvey Lodish, although that's not a bad reason, by the way. I'm an economist, after all.

See, I want to be Harvey because of what happened in 2002. In that year, Harvey's daughter was pregnant with her second child, Harvey and his wife's second grandchild, a boy named Andrew. Great name, by the way. Andrew was diagnosed in utero with Gaucher syndrome. What are the chances of that? So I talked to Harvey about this. I asked him. It was a very emotional conversation. I asked him, Harvey, did you know in 1983, when you started Genzyme, that you would be developing a drug that would someday save the life of your as-yet-unborn grandson?

And Harvey said, no. He had no idea. He said, I thought that if I could do some cool science, and help some patients, that would be great. 1983 was two decades before the human genome was sequenced. So I had no idea that I was carrying the mutation. And in 2012, when his son turned 10, he developed the full-blown symptoms of Gaucher's. So he would be dead if it weren't for the drug that grandpa developed. That's why I want to be Harvey Lodish.

I don't have an MD or a PhD in molecular biology. I will never be able to develop a drug that will save my as-yet-unborn grandchildren. But I realized something. I realized that you know what? We can all be Harvey Lodish if we invest in the drugs that save our as-yet-unborn grandchildren. Finance doesn't always have to be a zero-sum game if we don't let it.

With the right business models, the right scale at the right time, we can do the thing that everybody says they want to do, but very few of us ever get to do, which is that we can actually do well by doing good. And with your help, we can actually do this

[INTERPOSING VOICES]

[CRESCENDO]

Thank you. I teach MBA students, so I have to use sound effects. I'm sorry. Thank you. We have some time for questions?

PROFESSOR: Sure. Yeah.

ANDREW W. LO: Yeah, questions or comments? Yeah.

AUDIENCE: Yeah, [INAUDIBLE]. I know you mentioned about when you're talking about the [INAUDIBLE] partners, when you talk about the payout from 10 years, 11, to 20.

ANDREW W. LO: Yeah.

AUDIENCE: And you're saying that that [INAUDIBLE] is one month, how long does a patent last.

ANDREW W. LO: That's right.

AUDIENCE: So I was wondering after you said that, other people [INAUDIBLE]. I guess I wasn't sure about how that whole process works. But after you [INAUDIBLE]

ANDREW W. LO: Sure. So when you have a patent, it gives you the right to use the information in the patent exclusively, meaning nobody else is allowed to use that information. And so typically for drugs, what is that information? It's basically a chemical formula for a particular compound that doesn't exist in nature naturally. You created it, you came up with it, you filed a patent disclosure. And the patent office said, yep, this is new, and useful. We're going to grant you the patent.

So for 20 years, only you are allowed to use that idea. And so when you use that idea to create a drug, you're the only one that's allowed to make the drug. And so if people want that drug, they got to pay you. And so you end up charging a price for the drug that will generate a lot of value for you. At the end of the 20 years, what's the deal? The deal is everybody gets to use that idea. And so now, you've got companies that can produce the drug. Because typically, the producing of the drug is pretty cheap, right?

Once you give me the formula, I can basically get a chemical manufacturing plant to come up with it relatively cheaply, a few pennies a pill. The expensive part was developing the clinical trials to get the FDA to give you the license to do it. Once that's done, it's all profits for you until such time as now everybody gets to produce it for relatively low amounts of money.

So it's like aspirin. At one point, aspirin was patented. Now anybody can make it because you could look up the patent. There's the formula right there. You can do it yourself if you know how to mix those chemicals. And you don't have to pay anybody for it. But before the patent expires, you're not allowed to use the idea. Or if you want to use the idea, you have to pay the owner of the patent a fee for using their idea. That's how it works. Yeah.

AUDIENCE: How do you find these investment opportunities? How do you even begin to research these [INAUDIBLE]?

ANDREW W. LO: Yeah, that's a great, great question. The answer is you need to have expertise. So as I mentioned, Neil Kumar, the co-founder of BridgeBio, and the person who created it really, Neil has a PhD in chemical engineering. But he didn't go off and become a chemical engineer. He went off and first worked at McKinsey, advising biotech companies about their corporate strategy. And ultimately, he decided to start investing in various different ideas because he had the expertise.

As a chemical engineer, you have the science background, the engineering background, and then as you work in the industry, you learn about how the industry works. So you learn that aspect of it. That's what gives you the expertise.

And then once you have the expertise, the companies that have the money to invest, the venture capital firms, the private equity firms, even the big pharma companies that have corporate venture divisions, they will want to hire you to help them manage the money. That's how you ultimately end up being able to do that. You got to have the expertise.

And by the way, that's one of the reasons why MIT graduates are so popular among Wall Street investment houses, because you all not only have expertise, but you have the ability to learn and develop new expertise as needed. That's really important. Yes.

AUDIENCE: How do we invest in this?

ANDREW W. LO: What's that.

AUDIENCE: How do we invest in this?

ANDREW W. LO: How do you invest? Well, that's actually the same question I have. How do I invest in you? You all are the next generation of investment opportunities. And I'm not saying this just to flatter you. This is a biological fact. You are going to be around a lot longer than Jake, Peter, and I. And therefore, all of you are the future of innovation. And so, yes. I would love to figure out how you invest.

In terms of investing in these kind of companies, the biotech companies, well, BridgeBio is publicly traded. So anybody can invest. And I'm not suggesting you should invest in them. There's risk, very, very high risk, by the way, in biotech companies. So you need to be very careful about that.

But the much harder areas to invest are the private companies, because by definition, they're private. So you don't know as much about them as publicly-traded companies where you've got a lot of published information. And you probably are already aware, but if you're not, you should be, that MIT is an incredibly attractive place for private investors to come and look for opportunities among the students and the faculty.

You are in a wonderful position, particularly those of you who are majoring in math, because your skills are portable to virtually every industry out there. I don't know of an industry that doesn't need math. Maybe the Hollywood film industry. But you've got to count your money somehow. Tom Cruise has to count his money. So you got to have math for that.

So I think that there are lots of venture capitalists hanging around Kendall Square and MIT to try to understand whether they can invest in you. You will find that to be a very, very interesting phenomenon. Yeah, I'll come back to you. But you were first.

AUDIENCE: [INAUDIBLE] thing that you want to invest in, these groups already exist that are trying to use these things, but they need money. Or is it that the investment going towards starting XYZ that does this specific thing?

ANDREW W. LO: Well, there is still a valley of death in the sense that there are lots of groups that want money to do the kind of cool things that you are all going to come up with on your own. By the way, to put in a plug for Dennis Whyte, he teaches a course on nuclear engineering, where as part of the course, they come up with ideas, a number of which ultimately end up becoming commercialized and real startups.

So there are a number of companies that can't get funded because of the valley of death. MIT has a much better opportunity set than if you were, say, at Duke University or University of North Carolina. That's part of the research triangle down south. And they've got some really cool ideas, smart students, and faculty as well. But because they're not part of the Boston, Cambridge ecosystem, they don't have as many venture capitalists down there looking to fund various different projects.

So I would say that there are still lots and lots of smaller groups that are looking for funding that can't get it because they just don't know enough about the financing. So what I've described to you now, in just this one class, is probably more information than most startup groups have in terms of thinking about risk rewards, and trade offs like that. Yes.

AUDIENCE: [INAUDIBLE], you're also a professor here. So I was wondering [INAUDIBLE] and stuff like that here at MIT? Or is that something that [INAUDIBLE]?

ANDREW W. LO: So again, very glad you asked that question, because I happen to be teaching a class right now on health care financing. It's called 15.482. Now for those of you who may not be able to take that class because of conflicts or whatever, that class is actually online. It's part of MIT's Open Learning Library. So there is a version of 482x that you can all sign up for. It's free. There's an archived version of it. So just check on the Open Learning Library website. It's not part of OCW, but Open Learning Library. Yeah.

AUDIENCE: So the gentleman who started [INAUDIBLE], can you just give a rough outline of how on Earth he did that from a PhD? [INAUDIBLE].

ANDREW W. LO: Sure. So the first thing he did when he graduated was he went to McKinsey, a consulting company. And he knew a lot of science and engineering, but he didn't know much about the industry. As part of McKinsey's program, they train their hires to learn about the industry. So probably for the first year, he shadowed a more experienced biopharma consultant that brought him into various different companies and showed him projects that they were working on, and how he could add to those projects by doing research.

Just like if he were a chemical engineer doing research on better ways of refining oil, he'd have to go and read articles, and then talk to people, and then do experiments. In that same way, if you're in a consulting firm like McKinsey, and you're working on a project like, how should Pfizer fund their vaccine program for RSV? Well, what would he do? He would go and learn about RSV, he would read the journal articles, he would figure out how it's being funded now, he would come up with new ideas, he would try to test them out by writing different simulation examples to illustrate what could happen.

Those are the kind of things that he did for the first three to five years of his career. At some point, he learned enough about the industry to start making investment decisions, like, this company has got a good bet, because all the things that I was studying about proper ways of funding particular projects, they're doing it versus this company, I don't really want to invest because they don't even understand how to fund their internal pipeline.

So at some point, he left McKinsey to join Third Rock Ventures, which is a biotech venture capital company. And then he spent a few years there learning how to make investments. It was at Third Rock that he approached me and said, look, I've been thinking about rare diseases as well. I've seen investments that Third Rock has passed on because it's not a so-called platform technology. It's only a one-trick pony, one idea, one drug, one disease. And Third Rock thought it was too risky. Would you be willing to run some models with me to fund those projects?

And after we ran a bunch of simulations, it gave him enough conviction that this was going to be a profitable venture that he was willing to take the risk to try to do that. And the first thing we did was we asked Third Rock, you guys passed on these three opportunities. Do you mind if we take them? Can we invest in them? Third Rock said, be my guest. Go for it. And what was not appropriate for Third Rock, given they've got lots of other opportunities that they're focusing on, was a great opportunity set for BridgeBio, this portfolio company.

So like anything else, it's a gradual process where you learn more, and more, and more. And sometimes, at some point, you learn so much, that you are confident that you know enough to be able to start your own company.

AUDIENCE: That's great. Thank you so much.

ANDREW W. LO: Yeah, sure. By the way, it doesn't mean it's any less scary. There is still a scary moment where you've learned all this stuff, but still, quitting your job with a baby at home, and bills to pay, that is scary. But at some point, your confidence and your ability to get through that scary period outweighs the wall that your emotions put up. Yes.

AUDIENCE: I have a question about in times of crisis or when you actually need some type of growth, or for example like a COVID-19 vaccine or you need [INAUDIBLE]. I guess, because you talked about the [INAUDIBLE] and all that stuff. Is that during those times? How is it adjusted? I would say, or if you can get into how it's like [INAUDIBLE].

ANDREW W. LO: Well, so that's a really important observation, because in the case of COVID-19, we did have a valley of death. And we still do have a valley of death when it comes to vaccines, because the profitability of the typical vaccine is not very attractive. And so prior to COVID, most big pharma companies were actually getting out of the vaccine business. Cancer was much more profitable. Rare diseases actually ended up being more profitable than vaccines.

And so right before the pandemic hit, there were only four big pharma companies left that were still in the vaccine-making business. And but once the pandemic hit, and we knew that it was going to be bad, when it came on US shores in March of 2020, we knew it was going to be bad. At that point, a lot of things started to happen all at the same time.

First of all, philanthropy had been funding scientific experiments for vaccines for decades, in particular, the Gates Foundation. They, for years, have been working on a vaccine for malaria. Still doesn't exist, by the way. We still don't have a vaccine for malaria, believe it or not. Malaria is probably the single biggest killer around the world. Not here in the US, but in Africa, where malaria is a real problem for many, many countries. And it kills literally millions of people every year.

So the Gates Foundation had been working on that for many years, funding scientific research, and funding Moderna in particular, among other companies. And so once the vaccine hit US soil, we were very, very quick to be able to collaborate with international scientists to get the sequence, the genetic sequence, of the particular spike protein that we're going to target with the various different antibodies.

So that process worked like magic. There was no valley of death for that period of time, because the government stepped in and said, we got to do something, otherwise, lots of people are going to die.

For the very first time in the history of the industry, it took 63 days from the time we sequenced the COVID-19 virus to when the first human patient was injected with the vaccine candidate, 63 days. Typically, it takes three to five years to create a vaccine. It took us 63 days. That's an example of what you're talking about getting around the valley of death. The problem is now that COVID seems like it's over, of course, it's not really over. You can still get COVID-19, as many of you will find out in the next few months. But it's not as serious. We know how to deal with it.

We've got a number of drugs and treatments. And we recognize the various different symptoms. So because it is not that serious, people are more relaxed about it. And what that means is the valley of death is back. People don't want to spend money on it. They'd rather spend money on, guess what? AI. Right? Let's put money in OpenAI, or Anthropic, or any one of these other companies. And that's a problem.

So I think that we need to worry about that. That's one of the reasons why I'm here today, to try to get some of you to be excited about taking your ideas, and your toolkits, and doing well by doing good. You will really do spectacularly well, from a financial point of view, if you're able to succeed in fusion, or in drug development devices, and so on. But even more importantly, you're going to feel really good about what you're doing. And you're going to actually help a lot of people. All right. I'm out of time. So thank you very much, and have a good day.

AUDIENCE: Thank you.