FROM DISCOVERY TO DELIVERY: THE NEXT FRONTIER IN CANCER INNOVATION

Announcer

Thank you for joining us. Please welcome the panel to the stage.

Gregory Simon

It is my fear as an old man that I'll be on a desert island with a lot of food I can't open.

[Laughter]

Good morning. Thank you for being here today. Many years ago, the biologist-philosopher Lewis Thomas wrote a book called *The Life[s] of a Cell*. And today we're going to talk about the life of a *sale*. How do we go from an idea to a drug or a diagnostic that saves lives? And as we know, just as with human lives, there are a lot of roadblocks along the way from being born to being successful, or even staying alive in many parts of the world. We've got a terrific group of people today. Dr. Bar-Sagi here on my left has worked on the RAS protein forever, and I'm sure you're very excited about what's going on. Ken is at Daiichi Sankyo, which has a number of new drugs on the market that are moving therapies up earlier into disease progression. Isabel runs an organization that deals with how to get therapies into the cities that are usually ignored in many parts of the world. Greg Raskin spent many years in tech transfer at Sloan Kettering and now is at Royalty Pharma on the other side of that table. And AmirAli at Guardant started the first company to do blood tests for colon cancer screening that has now reached 300 million people that can now get that test and have it reimbursed. So, this is quite a crowd. I'd like to start at the beginning, just contrary to my usual style, and talk about the view of the world from the research lab in terms of when you look back at the work you did in RAS, and you look at how long it's taken us to get to where it's a druggable thing, what were the impediments in your day-to-day work that slowed it down? Was it money? Was it permission from above? Was it the researcher pool? And now with this attack on scientific funding that's been going on for two years, how does that bode for the future?

Dafna Bar-Sagi

Really great question, and I'm not sure that I am asking myself again and again, what was the real impediment in terms of moving from understanding how RAS is working to designing a drug? One thing that I think is important is technology, because some of the methodologies that have been used in order to develop the inhibitors from Kevan Shokat's days to now have not been in existence at the time that we just started to understand biochemically how this molecule is working—protein. So, we knew right at the outset that it's a GTP-binding protein, but beyond that, there was very little knowledge in terms of how it's regulated, how important is the GTP binding for the function of the protein. And once this was settled, which was a good decade, understanding what are the downstream effectors, what are the upstream regulators, that I think gave the platform at least to start developing the technology to generate the inhibitor. I think that it's just an amazing tour de force effort that really tells us a story which is not new. It takes a very long time. Just for curiosity, I looked at how long it took to get beta-blockers. Anybody in the audience wants to give a guess? It's 25 years—

Gregory Simon

Wow.

Dafna Bar-Sagi

—from Sir Black's initial discovery. Same thing for antibiotics. So, it's not rare, but I think that that's part of what we all have to take into account. It's even not necessarily fundamental science leading to applicable end results. It just takes a very, very long time, and I don't think that it was even a question of funding. I think, in my opinion, it was the first realization that it's possible. And then once you make it, then you are able to move on.

Gregory Simon

So, you had to believe you could see it to see it. Basically.

Dafna Bar-Sagi

It is very true.

Gregory Simon

So, from a lab at NYU, your next step would normally be the licensing office if you think you had something valuable.

Dafna Bar-Sagi

Correct.

Gregory Simon

How did you view the licensing office? I'm setting you up here because I'm going to ask him the opposite question. How did you view that next step? Did you view it as a pain? Did you view it as an opportunity? Did you view it as they're going to argue with everything I say? How did you view the tech transfer office?

Dafna Bar-Sagi

I think the tech transfer offices, of course, they run slightly differently in different institutions. I think that the process can be much more nimble in terms of regulatory requirements, and also alignment between industry and academia could be better in terms of how we march together, as opposed to this transactional relationship where you create something, and then you have to decide who is getting what part of the creation. A lot of opportunities. So, for us, it's probably as cumbersome as it is for most tech transfer offices in an academic institution. And I think it's a lost opportunity for society in general that there is not a much smoother way of moving from the lab, if you have a great discovery, to people.

Gregory Simon

Yeah. We have a countdown clock here, and most people don't live with a countdown clock until they get diagnosed with cancer. Then they have a countdown clock. And most people don't realize that that countdown clock—"Well, why does it take so long to get the trial done? Why does it take so long to get the medicine to me?"—starts at the university in the tech transfer office. Forty years ago, when I moved to Washington, I was on the House Science Committee when they passed the Bayh-Dole Act, which opened up the door to the modern tech transfer world. There's been a lot of controversy about that. So, Greg Raskin, you spent many, many years licensing out of universities. Discuss how you felt when people brought new ideas to you, and feel free to discuss confirmation bias, greed, irrational expectations. How did you view that initial conversation, and how often were you surprised that things were better than you thought?

Greg Raskin

Wow. So, I loved working in tech transfer. I thought it was a super interesting job. You get to talk to brilliant scientists every day, like the good doctor over there, and learn about all different kinds of potential medicines. Where I used to work at Memorial Sloan Kettering, we had the ability to have an idea come from someone's head in their lab and take it through all the trials you need, the laboratory experiments you need to prove to the FDA that it's safe enough to start in clinical trials. And actually, we had an IND writing corps. We could actually write the applications to the FDA and start those drugs in our own patients. So that's a pretty special place to be. It was a pretty exciting opportunity. So, I was delighted when any physician-scientist came to talk to us about a new experiment that they were working on, a new idea they had. Sometimes scientists can be divas. They are these brilliant people. They run their own labs. Sometimes they would think that they were the one true genius surrounded by a confederacy of dunces, and I was the chief dunce, maybe. But that's okay. I was able to put down my own ego for that because it was just so exciting to be able to bring these new technologies into our patients to try to help them. We were able to develop drugs at Memorial Sloan Kettering. Memorial Sloan Kettering has developed more drugs that were approved by the FDA, at least when I last looked—there was a *New England Journal* article—the third most drugs of any academic center in the United States. So, number one was the NIH. Okay, well, there's Dr. Collins there, so that doesn't seem fair. That seems like a big organization. Number two was the UC system, all of the University of California, and number three was Memorial Sloan Kettering. So that was a remarkable place to be doing this job. Yeah. So, I don't know about greed. I think we did a good job of getting these things to patients, I think. I got to work with a very good team and really great scientists.

Gregory Simon

In the early '80s and '90s, early days of tech transfer, there wasn't quite as developed a VC community, and certainly an investing community, as there is today. How did that change during your tenure?

Greg Raskin

When I got there, I didn't start in tech transfer. I was an investor before that, and I was a physician before that. And because I was an investor, I sort of knew what the end user was going to look for when you were developing a product or doing a deal. And so, I came about it, I think, with maybe a slightly fresh perspective, or maybe there were a few other folks doing it the same way. Previously, royalties were the main coin of the realm. So, if you had the tech transfer office, you had the Bayh-Dole Act rules, you were responsible for protecting your IP, protecting your patents, and then trying to commercialize it, trying to develop that technology, and in exchange you'd get royalties. I saw this VC community building, and having been one before, I thought, "Well, I don't want all of those people to just get rich at the expense of our institution. It's my job to bring in value." So, we started to take equity in these deals as well, and I think now that's pretty common when people start companies. At the beginning, really, it was mostly just royalties. So that's the way that we interacted with the venture capital community.

Gregory Simon

Thank you. Isabel, let me leap to the view from the street, so to speak. We're talking about the beginning of drug development and therapy development, and yet you work with the people at the other end of the chain. When do you get to make your input into what is needed, how it should be addressed, what patients' concerns are? Do you ever get involved at the university research level, at the early commercialization level, or are you only waiting for the products to come out and then hoping they can be affordable and accessible?

Isabel Mestres

Wow. That's a great question. We're not sitting at that table. Local people are not sitting at those tables. Local people are not sitting at those tables. And I'll come back and elaborate a bit more, but let me put a bit of—because I think I bring a very different perspective from this panel, which I think is an interesting perspective. So just to put on, there are 9.8 million people dying every year of cancer. 70 percent of those deaths are in low-resource settings. Less than 50 percent of the countries don't have access to basic diagnostics. There was a *Lancet* paper that says that out of these 9.8, 4.5 million cancer deaths could be avoided. So, what happened is we're talking about a lot of innovation, massive investments. I was reading recently, 80 billion go into oncology and research, but very little, like 1 percent of that, is going to implementation. So, for who? I would like to *[Inaudible]* this room. Who are we innovating for? Are we innovating for the few, or are we really want to have an impact to people? Because if we talk about what's the next innovation frontier, for me, it's a no-brainer. For WHO, it's not a no-brainer. I was recently with the World Bank. It's not a no-brainer. Implementation. Health systems are not absorbing this innovation. And even high-income countries, if we don't balance the proportion of innovation of these incredible treatments with innovation of systems, there's not going to be a market. And the most important, we all work here, or we all want to impact people's lives. Well, we're failing because we're not putting the money where the money's needed, which is now it's time for those systems to absorb the innovation and be as lucky as all of us in this room that have systems that are supporting us. And that takes us to my role at City Cancer Challenge Foundation. For all of you that don't know, we were born in Switzerland by the Union for International Cancer Control because the cancer community was, actually there is a massive gap in

how we bring this innovation to people that need it, and that's why we were created. So, we're working with more than 23 countries across Africa, Latin America, and Asia to support the government to improve the health system. In order to do that, because it's very challenging to see it from a full perspective, we do it from a city level. Because in a city, we're able to see the whole continuum of the patient journey and stop looking at it in silos and vertical approaches. So, in a city, we can track from primary, secondary, tertiary, university, reimbursement systems, government policies, patients. We bring them all together and go step by step through the journey and really understand where the system breaks. Is it workforce? Is it finances? Is it data? Is it quality? Is it processes?

Isabel Mestres

That doesn't require massive investment. They don't need new hospitals. They don't need new technologies. They don't need new machines. They have it. What they don't have is processes. They don't have quality. They don't have the workforce, and that can be solved. And that's how we take it from discovery to delivery, from the ground at the city level with the end users, moving it from there to national policy, and that is what City Cancer Challenge is about. We work with massive partners. We work with ASCO. We work with the American Society for Clinical Pathology and many associations that are helping us to bring this incredible innovation to the patients that are in need. And again, to your point, it's not only the drug developments, also technology. We have a great partnership with Siemens Healthineers. We work very good, and the first thing I told the CEO was, "You have to stop innovating Ferraris for the desert." Innovation has to solve problems on the ground, and the first thing they wanted is to bring people from the ground to build innovation that suits the majority of the people. That's the big market. It's not these few high technologies that only a few countries can support.

Gregory Simon

Thank you very much. One more question for you, Dr. Bar-Sagi. We're all familiar now with the financial cuts to research. But the kinds of people who want to address what Isabel just said are the young researchers who are getting into the business of science because they want to solve problems like this. How is the current cutback affecting the availability of new researchers, and how long do you think it will take us to get back to where we were, much less where we should be?

Dafna Bar-Sagi

So, it's a very interesting question from a timing perspective because obviously the current cuts were affecting the ability of labs to grow, and that, of course, was very discouraging for the new generation of people that considered a career in biomedical research in academia, I have to emphasize. So, it was definitely a decline that we are seeing in terms of just people that are interested in being scientists in an academic medical center. I do think that it will calibrate itself because I feel that AI is going to change dramatically operations of research, and that's not going to take many years. It's going to take probably already next year. We can see what we can do without necessarily increasing. Every lab now can produce the equivalent of what you would need usually three or four investigators. So, I think that definitely, acutely, there is an effect, and we are seeing it. To me, it's really more a question of a little bit of loss of enthusiasm that came with that. Usually, as a scientist, in order to be successful, you have to be passionate, you have to be enthusiastic. There was a real, almost a mood effect on how researchers thought about the prospect of being successful, particularly since we all know that for discovery, you have to have sustained funding. Impactful discoveries can take years. There are ups and downs. You have to

take risks, and this does not lend itself to a funding landscape where you really kept at something for a limited amount of time, and you just have to stop midway and say, "Well, I have no more resources that I need to do." So, I have to say that we all adjusted to it in different institutions. We all found ways of managing it, and I guess we just have to see how things will unfold within the next few years.

Gregory Simon

Yeah. Before we get to the makers, Ken and AmirAli, I want to ask Greg one more last question. Now that you're at Royalty Pharma, how do you view your old environment, the tech transfer offices? Now you're buying, not selling.

Greg Raskin

Now I'm buying, not selling. That's right. Well, my job specifically is to be the sort of liaison to academia. So historically, Royalty Pharma actually did—our business is we buy royalties on individual medicines. So, it's an investment firm, but we don't invest in the stock of companies. We invest just in royalty streams from individual medicines. And historically, a lot of that work—the firm is 30 years old—but so, say, 30 years ago to 20 and 15 years ago, a lot of that work was with academic centers. In fact, we bought a big royalty from NYU for Remicade for $650 million, probably 20 years ago or something. And what we provide is, we provide the ability for a university or a medical center or a not-for-profit to use money that they could get right now instead of some potential future cash flows coming in every year. They can use it now for capital needs or to fund research. So, for example, before I got to Memorial Sloan Kettering, in 2004 and 2005, Royalty Pharma bought MSK's rights to royalties in Amgen's Neupogen and Neulasta. These are drugs used to rebuild your immune system if you're a cancer patient. And that money was used to build a building which, at the time, was the largest new research lab building in New York City. And they were able to put all that money to work at the beginning. So, I hope universities are successful in developing drugs. I hope they get good royalty streams, and then I hope we can help them finance. So that's what it's like to be on the buying side rather than the selling side.

Gregory Simon

Well, my immigrant grandfather always told me, "Don't say what two and two is unless you know if you're buying or selling." So, AmirAli, you have done an amazing thing against all odds. We have a system that prefers to lose 90 people to avoid bothering 10 people that we get wrong. So, for a long time, we wouldn't reimburse, we wouldn't recognize screening that involved a blood test or other biomarkers because we didn't want to have false negatives and false positives, and meanwhile, we had a lot of positives that didn't get detected, especially in treatable cancer like colon cancer. So, you have touched all of the rough spots of the system. Does it work? Should it be reimbursed? How do you get it to people? How does it relate to traditional diagnostics? How do we change the mindset that we need to be looking at more and more people to find the true negatives and the true positives and learn how to reduce the false negatives and positives? But you can't do that if people aren't reimbursed for the test that can be refined. So, can you talk about what was, in your mind, the breakthrough that allowed Guardant to get to where you're now available to 300 million people? And as a follow-up to that, I'd like you to talk about how many people who could be tested are being tested, and of the ones that are being tested, what is the success rate today?

AmirAli Talasaz

Yeah, very glad to be here. Very broad set of questions and important questions. And maybe I even start on the innovation part and discovery, but the reality, to your point, innovation is as impactful as our access operating system. If these innovations that a bunch of people have developed don't get global access, even in some of the best countries like the United States, people cannot get access to innovation in a timely way. We are limiting the impact on innovation, and we are going to limit, actually, the amount of investments which is going to come in the future generation of innovations. But starting from even at the top of the funnel, discovery, when we are looking at the disease biologies, there are many diseases that still there's a lot of unknowns about them. But the good thing is that landscape is changing. Our experience in the field of oncology and cancer has been like that's a field which has been data-starved. And as a community, we learned some of the effort, like the TCGA effort. It's kind of now ages ago, but still, even today, is paying off and paying dividends for us. The point is, this is the field that was data-starved, and as a result, we were not understanding biology, and it was impacting the way we are developing diagnosis and probably even developing therapeutics. Fast-forward right now, there are millions of patients that have been profiled comprehensively by us and other players. And those kinds of data are feeding into understanding the biology better, that now some kind of new classes of even therapeutics are coming. Putting AI on top, like there are some AI-based new therapeutic developments which are happening. We'll see what comes out of it. But even on the diagnostic side, we are seeing that when you're capturing high-quality data at masses, you use these new AI and analytical tools, you can develop diagnostic tests that are more sensitive, can detect diseases earlier, and even some diseases that previously we didn't have even any way to detect them. But now connecting it to your main question, the state of the union of innovation, I think, is very strong. But again, the main point is accessibility. I'll give you an example of a product that we launched, like, I don't know, maybe 12 years ago, for advanced cancer management, profiling, and treatment selection in those patients. Literally took us 10 years to get to a point that 300 million people in the US have access to it, or we are present in like 60 countries in terms of accessibility. Why did it take all that long? It was not because of FDA approval. It was not based on clinical utility. It was the operating system of accessibility. Now talking about even prevention, early diagnosis.

AmirAli Talasaz

We got the first FDA approval for a blood test with primary colorectal cancer screening, which is rising in young patients, became the number one cause of death, mortality in young patients. By the way, if any of you are over age 45, to really do colorectal cancer screening, and there are multiple choices and options. Gold standard is colonoscopy. But we've seen as a community, when there is a little bit even out-of-pocket cost for the patients, the amount of adoption of preventive services drops down significantly. We take it to the global level, even what you mentioned earlier, when the test is just costing a lot for the patient, the amount of utilization is going to be impacted heavily. Why shouldn't we have a better access system to make sure guideline-recommended solutions really get equitable, broad access? That's actually, I think, the future that we are seeing, and the future could be very bright if we make the access operating system better than what it is today.

Gregory Simon

I'm stealing that phrase. I love that phrase, the access operating system. That's excellent. Can you talk a bit about the Shield Across America tour, what that is?

AmirAli Talasaz

Yeah. So, our Shield blood test is our blood test for cancer screening with the first FDA indication for colorectal cancer, and when doctors are interested, patients interested, they can opt in to.

[Audiovisual pause]

Ken Keller

As you move it earlier and earlier, instead of adding months to a patient's life, our hope is that we could actually deliver more cures to patients. And so recently, earlier this year—I think I'm back on—

Gregory Simon

You're back—

Ken Keller

We received approval for this drug in both the neoadjuvant and the adjuvant setting in HER2-positive metastatic breast cancer. And so there the hope is—neoadjuvant is simply this: a woman is diagnosed early. That woman typically will receive some kind of systemic chemotherapy and IO, and then surgery. After surgery, what the physician wants to be able to say is, "I cannot find any cancer left." It's called a pathological complete response. That's what everybody wants to hear. And with this drug, we were able to increase the pathological complete response rates to about two-thirds of women. All right? So that's the end goal. That's really where your drug can have the biggest impact. But there's a bunch of challenges in that. For this disease, you're identifying HER2-positive breast cancer. That's fairly easy because there have been drugs that targeted HER2 for years. But we have other drugs we're developing where it's a brand-new biomarker. Right? We're actually developing drugs where it's not just the typical IHC biomarker. We're using digital pathology and AI to measure the expression of protein, not just is it present and how much, but where is that protein? Is it just in the membrane or inside the cell? And that's going to allow us to actually identify what patients can benefit from that drug. No one in the world, at least very few people in the world, have the equipment to do digital pathology routinely today. Right? They just don't. And so, it's not just the drug. We have to create the environment that people can be identified. Super important. And then the second part of your question is, with all medicines, there are side effects. Within HER2, there is a side effect called ILD. The risk-benefit is very different when you're looking at metastatic disease than early-stage disease. And so that bar to ensure that you're educating the physician community, the nursing community, the patients themselves to be aware of the most early signals or signs of that toxicity, that's incredibly important. So, we've actually redesigned our entire customer-facing company. And so, when I grew up in the industry, you would have salespeople, and we still have salespeople, but they're about that much compared to the other people that are touching customers. Today, we've got nurse educators that work in the field to make sure things are going the right way. Unfortunately, we have lots of people working on access and reimbursement in the US and other places as well. We've got pharmacists that are working in terms of the right dosing. So, we're surrounding the end user with the best support we can possibly bring. And all of that gets harder as you go earlier and earlier, but the benefits are much bigger.

Gregory Simon

Now, you partnered with AstraZeneca on a lot of your work. And also, universities. What are the challenges in those two different environments for collaboration in drug development?

Ken Keller

Yeah. So—

Gregory Simon

One second before you answer. There's a QR code. You can shoot me a question, and I may or may not use it, but feel free to shoot it. Go ahead.

Ken Keller

So, our thought process, we've got seven different antibody-drug conjugates being tested today to approved. We made a very simple decision early on. When we looked at the opportunity that these drugs provided, our question was, can we develop this drug ourselves and execute all of the clinical trials and everything else that goes on for all the potential indications? Right? And you have to look in the mirror and say, can you really do that? And how long would it take you versus how long would it take you and AstraZeneca, for example? We made the decision that it was a net benefit for everybody, patients, the oncology community, and us to work together. And to give you an example, Enhertu now has 11 different indications. Trust me, if we did it ourselves, we'd have maybe three or four. Right? So, partnering is always painful because it's your baby. I don't want to partner. But at the end of the day, the question you have to ask yourselves, can you get this drug to as many patients as possible, as fast as possible? Can you do it yourself, or do you need partners? We needed partners. In terms of working with universities and early on, we do a lot of outreach, typically through our, what we call, early development BD team, business development team. And they work with people, universities all over the world to try to be connected to the latest and greatest. We formed a number of research centers in Cambridge, here in the US. We've just opened up one in China because there's so much going on in China, and their job is to be connected to the early work and see if it makes sense for us to partner with them.

Gregory Simon

What is the challenge for you to collaborate with Isabel and in the local community?

Ken Keller

Well, we have a meeting right after this, so—but success is not getting the drug approved. Right? That's a celebration. That's awesome. That's great, and we do celebrate it, but we're not celebrating—that's not success. Success is getting it to patients. And we're kind of blessed in the United States because when a drug is approved, patients can access these drugs very quickly. We can talk about problems in our system and things that need to be fixed, but that is one of the things we have to preserve. And the truth is, that doesn't exist in many other places across the world. It is not unusual in Spain or Italy or the UK for medicines to be approved by the regulatory authorities, and patients can't get access to that drug for a year, two years. Right? And so, we have to work together to really make it better.

AmirAli Talasaz

If I may add something?

Gregory Simon

Yes, please.

AmirAli Talasaz

I think it would be good for us to think about how could we increase the access to prevention similar to the access that we have developed in this country for therapeutics. It was an interesting NIH modeling study that got published recently that they looked at, what has happened during the last 45, 50 years in some major cancer types, lung cancer, colon cancer, breast, prostate, and so on. And what they found, we averted or reduced about six million cancer deaths during the last 45 to 50 years, cumulatively. Last 45. And out of which 80 percent is because of prevention, early detection. The other 20 percent is because of other advancements, including therapeutics. Nothing wrong about—and very exciting stuff happening on the novel therapeutic development and some of the work that even we are doing with 200 pharma partners that we have. But sometimes we are not putting the attention that really prevention, early detection requires. Less than 3 percent of our health-care expenditure right now is going toward prevention and really true health care. Vast majority is going toward sick care.

Gregory Simon

Yes, Isabel.

Isabel Mestres

I want to build on the challenge of working in partnership. We're very grateful for Daiichi Sankyo because they're supporting our work, as also other companies in the room. I think Merck is around, also a partner, Amgen. The challenge we face in terms of getting investors or philanthropies to support our work, and I don't know if there is a philanthropy in the room or investor, please reach out because I'm really eager to get support, is return on investment. How do we measure impact? Traditionally, these philanthropies, you think Gates and the big health philanthropies, are used to communicable diseases. Number of vaccines, number of diseases prevented or kids. And a lot has been going through screening, because in screening, number of women screened, potential women with cancer. But that doesn't lead to any impact itself if there is nothing after. So traditionally, philanthropy is looking for quick return on investments, quick numbers that we can report. The challenge we face in oncology is that there is no one single thing that is going to actually impact the life of the patient. So, it's a huge journey. So how do we measure impact in oncology is one of the biggest challenges we have as a foundation or an NGO to get investment, because they're looking for numbers that are real. I cannot give you a number of how many people's lives we've saved. That would be very irresponsible from my side, because this is about—so we're looking to—we work with King's College and WHO to develop the first-ever quality cancer care indicators for low-resource settings. There was none.

Gregory Simon

Wow.

Isabel Mestres

None. We had to be like a little NGO trying to push WHO to come up with quality cancer care indicators, and we're the ones actually implementing because we are the ones on the ground. So, we're now measuring things like how many women are we downstaging for breast cancer? What's the time from

screening to actually biopsy? What's the time from diagnosis to treatment? What are the abandonment rates? We're struggling to get data to measure these types of indicators. And that is something that we're putting a lot of money, but it's hard money because it's not sexy. I cannot say, "Oh, this is a new hospital. Voilà, come and cut." We need to actually strengthen these systems and these things on time, processes, quality. That's what we need to invest, and that's what's going to actually come with the return on investment. But it's a long-term investment. And that's the other thing. Donors want one-year investments. One year, voilà. How many patients? So, we really push, and we're hopeful, companies like Daiichi Sankyo, it's a three-year, it's a five-year partnership, and it's hard for them. But once they understand that this is a long-term game, and I really think we have to educate philanthropists that this is not about shiny numbers, brochures anymore. That is over. There's been a lot of money thrown into these low-income countries to just get nice numbers into a brochure, but not real impact. And I know it's not sexy, but I really would like all of us to start being more conscious of how the money is reaching outcomes and not making us look good with good numbers.

Gregory Simon

You may have to open an office in America because we just killed the Agency for Health Research and Quality, the Agency for Health Resources and Services Administration, because you can't improve things you can't measure. And if you can't measure it, how's anybody going to complain about it? People don't realize that if we stop looking at the results of our investments, people will stop wanting to make those investments because they won't see the impact. So let me add a question from the audience to a question that we all have, and that is the impact of clinical trials going to China and the role of the individual physician in bringing the changes you are developing to the patient. So, if trials happen in China, patients here aren't in those trials, and their doctors won't be referring people to those trials or even be aware necessarily of those trials, especially the failed ones. So, what is the role of the local physician who's already encumbered by incredible burdens in terms of dealing with all the patients, especially in low-resource areas? What is their role, and how do you work with them to bring these innovations to the local doctor, and how will the exporting of clinical trials affect that? I'll start with you, Ken.

Ken Keller

So, if I look at my own company, Daiichi Sankyo and if I look at our oncology trials, less than 10 percent of the patients come from the United States today. And like everyone else, we're doing trials all across the globe. I think China has systematically created an infrastructure that today they can enroll patients much faster than we can, and the gap is getting wider and wider. Now, we always have a stopgap because you're not going to get drugs approved in the US unless you have a certain number of patients. But it is difficult today. And so, on the individual physician level, I think they can only enroll patients if clinical sites are open in their area. And so, we do a lot of work to try to open up clinical sites. But of all the things that are getting better, regulatory filings are getting better, faster, quicker because of AI. Clinical trials in the US, I personally haven't seen that getting better, and so I'll just stop there. Yeah.

Gregory Simon

Amir?

AmirAli Talasaz

Maybe I can add something. Yeah. So, we are working with a lot of pharma partners, but I'll just give the example of what we are seeing even in diagnostics and why some of the trials are moving away from the US. We did a major colorectal cancer screening trial in the US, 40,000 patients, and it was all US-based. A few years after, we started a 12,000 lung cancer screening study, and we are enrolling two-thirds outside of the US, frankly. And what's the reason? I can tell you it's not cost. When you're looking at some of the issues that we have in this country, how quickly a trial can start, and after that, how quickly we can enroll. It's not because of patient flow. Some is because of some other bottlenecks. Removal of those bottlenecks is very important. It needs major public-private health system partnership. Here, you want to start some trials, you have to go and individually contract with some of the major health systems one by one. Just look at how long it could take, how long it could generate additional cost, but more important, time. We take some of the trial sites to Europe or Asia. The infrastructure is much more suitable. And at the end, some of the impact would be on the patients who are not going to get maybe enrolled and access in the US. But I think it's more of really a pharmaceutical kind of an issue than diagnostics.

Dafna Bar-Sagi

But I would just add, just because we have been dealing with that internally with activation time. Yeah, of course, if you're going to have a global or national solution, it's going to be maybe better. But I don't think that it's impossible for each—I think it has to be an expectation that each system should have a process that is really much more nimble because it is really—you know that the drug is available for a trial. You know that you have a class of patients that can benefit from it, even in the context of a trial, and they cannot get access to it just because of the bureaucracy that goes around this whole thing. So, I agree there has to be initiative, but it doesn't cost a lot of money to improve it. It's just really operations. But you're definitely very right. I was horrified when I started to look at our data. It's going to take 150 days, 120 days. It's just not good.

Gregory Simon

So, there are a couple of questions I'm not going to be able to get into that I just want to list. One of which is, as we get more and more subdiseases, how does that affect the finance of development? As we get more and more AI involved, how does that affect the cost of development? But I do want to ask this question before I get to your final question. If AI is going to reduce the cost and the time of drug development, and AI is based on the data of all of us, who is going to get those savings? Is it just going to increase the margin of the developers? Or will this finally be a point where we can say we can lower the price of drugs because the AI technology has lowered the price of development and put that saving into society? What are your thoughts on that? Anybody.

AmirAli Talasaz

I can start actually again on the diagnostic front. And what we are really experiencing, again, vast amounts of data have been captured. With these AI advancements, I can tell you we are seeing benefits on two fronts. One is what maybe you're hearing very frequently: The productivity of some of the best scientists that we have has improved. And we are seeing that. They all have these agents next to them that are really adding to the productivity that they are showing really on a weekly basis. Like a good fraction of our software is getting built now by some of these AI agents. But more importantly, and probably more impactful, is AI plus high-quality data is enabling us to make advancements in diagnostic development at a much faster pace. Like today, if you ask me, "AmirAli, did you envision that today, with your blood test, not

only you would have proof of concept to look at oncology signal, but you can look at some other diseases in the same blood test?" I would say probably we would be a few years still away from it. Now, again, this is pipeline, not ready for prime time, but we are seeing when we are doing this blood test, not only are we finding early signs of multiple cancers in the patient's blood, we are finding signs of some other disease at an early stage in the same blood test. That has been powered by AI. How to bring that kind of a benefit to the end users and patients, I think acceleration of these advancements definitely generates a lot of patient value. In terms of pricing, some of the work that we are doing is just additional algorithm and software, and the indication can, over time, get expanded for some of the tests that we are doing. Necessarily, we don't need to adjust our pricing when we are adding additional clinical value to the patients.

Gregory Simon

So last question. When we did the Cancer Moonshot in 2016, we only had nine months. And everybody, especially the press, said, "What can you get done in nine months?" Well, nine months was half of the life of my friend with GBM, a third of the life of my friend with multiple myeloma. So, my answer was, you can get a lot done in nine months, and patients deserve us to get a lot done in nine months. So, between now and this session next year, what is one thing that you can get done that we've discussed today to improve the life of patients, and what would you have to do to get it done? And I'm going to start with Ken. I'm going to hand it to you, Dr. Bar-Sagi.

Ken Keller

Sure. A year from now, I hope I can tell you that the three key clinical trial readouts that we have this year for patients with non-small cell lung cancer, I hope I can come here and we can be thinking about, okay, how do we get it paid for? Right? Because it works. We can figure out that part. So that's what I hope happens.

Gregory Simon

AmirAli?

AmirAli Talasaz

I would say the state of the union of innovation is very strong, and the future would be bright from an innovation perspective. But as we talked about earlier, the impact would be limited by the accessibility of these innovations. So, our commitment and what we are focused on is working on some of the initiatives to make sure people can get broad and equitable access. We can do our part, but we cannot change some of the policies or make sure a guideline body funded under HHS meets finally after two years when they have not met during the last two years. Right? So, some of the work is limited with what we can do, but we are going to do our part, and we are going to continue the hard work for the sake of patient benefit.

Gregory Simon

Greg, what's your goal in Royalty Pharma?

Greg Raskin

Sure. My personal goal is I hope that we can, over this next year, provide financing to universities or medical centers who can put the money that we provide to them back into research to fund the work that we need to do to help cure cancer.

Gregory Simon

Isabel?

Isabel Mestres

Look, I'm going to take the stage to get my opportunity. So, we work in 23 countries in low-resource settings, low- and middle-income countries. What I would like in one year is actually explore a city in the US. I think there are disparities here. There are some places with low-resource settings and disadvantaged people. I want to test our model in the US. I'm really looking for partners, donors, and I would like to announce next year our first city in a high-income country targeting vulnerable populations, and I think our model would definitely be a success here. So that's what I'm going to work on. Next year, announcing here a city in the US.

Gregory Simon

I'll take you to my hometown, or southeast Washington, which have the same problems, actually. Dr. Bar-Sagi, I'll leave you the last word.

Dafna Bar-Sagi

So, I think that what has become apparent, at least towards the latter part of the session, data is going to be the major currency that all of us are going to have to use in order to move in any sort of direction that we want to improve the delivery of discoveries to patients. My hope there is that we're still very siloed between different institutions, between different organizations in terms of data sharing, and that's a huge loss of opportunity. Not only because the more data, the more chances that all these models that we're going to build are going to be much more predictive, but also data represents different care modalities in different systems, demographics, all these things that we need to understand. So, this is one place. And then the other place that we didn't have a chance to discuss is we all read the amazing journals, and we have every week about 20 or 30 discoveries published. Why are many of them never getting from the point of a discovery or a nice paper to the patient? And I think we really need to reverse the vector from bench to bedside, from bedside to bench. I mean, really, the research that we're doing in the laboratories has to be informed much better from patient challenges that we need to solve, because otherwise, the research system is investing a lot of money in beautiful research, and it doesn't even have to be fundamental versus translational. But if this research, if the problem forming is not informed by a clinical need or a patient need, just a lot of resources are going to be spent not in the best possible way.

Gregory Simon

Thank you for your attention, and thank our panelists for a great discussion.

Announcer

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