Transcript with Mike Rockefeller and Leonard Schleifer Regeneron: Betting on Science and Saving a President

Recorded May 6, 2026

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LEONARD SCHLEIFER

Given what we know about his condition and the virus, etc., that he had a very high probability of dying. When you save any life, it's important when you save the President of the United States, it became quite the story.

MIKE ROCKEFELLER

Regeneron is one of the oldest and largest founder-led companies in the S&P 500. It's up there with the giants like NVIDIA, Blackstone, Oracle, and Dell. It was founded in 1988 by Dr. Leonard Schleifer, its president and CEO, and Dr. George Yancopoulos, its president and chief scientific officer. Len and George have been in their same roles for 38 years.

LEONARD SCHLEIFER

They thought we were going to sell maybe 100-something the first year, but we sold 800 million. And it seemed like, oh my God, this is the real deal now.

MIKE ROCKEFELLER

Today, we sit down with Len to talk about Regeneron's history, its key products, and how its deep pipeline will position the company for success in the future.

LEONARD SCHLEIFER

I don't think we get any credit for our pipeline because if we take your revenue projections for Dupixent, you get all your value back from Dupixent, not to mention the $18 billion we have in the bank.

MIKE ROCKEFELLER

For investors, by an investor. Conversations with executives building tomorrow's great companies. You mentioned liver disease. And as I was going through your pipeline, and you have a couple phase two assets for MASH.

LEONARD SCHLEIFER

Yeah.

MIKE ROCKEFELLER

Which ones are you most excited about?

LEONARD SCHLEIFER

Ones I haven't told you about. Stay tuned.

MIKE ROCKEFELLER

I'm Mike Rockefeller, co-chief investment officer of Woodline Partners, and this is inSpired. Well, great to be here, Len.

LEONARD SCHLEIFER

Good to have you here, Mike.

MIKE ROCKEFELLER

Has it sunk in yet that you are coming up on 40 years since you founded the company?

LEONARD SCHLEIFER

You know, it doesn't seem like 40 years on the one side. And on the other hand, sometimes it seems like a lot longer. But, you know, when you're doing something you love, time just passes.

MIKE ROCKEFELLER

Take us back to 1988 when you started the company, what the vision was, and maybe how that has turned into what Regeneron is today.

Founding Regeneron in 1988

LEONARD SCHLEIFER

Yeah. It's been a long time. And you mentioned Warren Buffett, by the way,

before we get to 1988. So a couple of people in my family keep track of who's the longest continuous serving CEO of a large public company. And that was always Warren Buffett, Warren Buffett. I just ran into Warren at a conference and I thanked him for retiring because that moved me up in the longest serving CEO continuously of a public company. But back in 1988, you know, I completed a lot of training. If you think about it, after college, I did seven years of training as an MD-PhD with a fellow by the name of Al Gilman, great, great mentor of mine, Nobel Prize winner. Unfortunately, he passed away a few years ago from pancreatic cancer. But I had great training with Al, so I got both my MD and PhD. And then I decided that I still wanted to be a doctor, a real doctor, not just a paper doctor. So I spent four years in residency with internal medicine training for a year and then neurology training where I became a board-certified neurologist. I was on the faculty at Cornell. I was doing research. I had a lot of grants, startup grants, NIH, American Heart Association. But as I was reading the literature, all the exciting work seemed to be about molecular biology. And I

had been trained as a molecular biochemist, not a molecular biologist. I didn't do gene cloning or any of that stuff. And then all the great papers seemed to be coming from this company, Genentech or Jane Tech and Genentech, of course, as they call themselves. I said, what the heck is that? And I said, well, that's interesting. there, a biotechnology company that are trying to come up with treatments for important diseases, taking advantage of the new science called molecular biology and molecular cloning. And so I had this notion about starting a company that would sort of try and imitate what Genentech was doing, but do it in the context of neurobiology, neuroscience, because I was a neurologist. And I thought that what were they working on? They were working on things like human growth hormone. And then this company Amgen was coming along. They were working on EPO and Neupogen. And I said, you know, maybe the nervous system is just as complicated as the hematopoietic system. Frankly, obviously, I thought it was more complicated. And there was only one nerve growth factor known at the time, NGF. And I said, you know, there had to be more. And if we could clone them and make them and spritz them on people whose neurons were dying, maybe we could treat degenerative neurologic diseases. And I started thinking about that. And my mentor had called, Al Gilman. I said, Al, what do you think about this? He said, it's the stupidest idea he's ever heard from me. And he says he's heard a lot of stupid ones over seven years of training. But when he realized that I wasn't going to be talked out of this, he said, all right, if you're going to do this, let's do it right. And he recruited a couple of Nobel Prize winners, Brown and Goldstein and Arthur Kornberg and Eric Shooter. We all got together and said, let's do this. And so I started this company called Regeneron for regenerating neurons. And the idea was to come up with new neurotrophic factors. The only problem was I wasn't a molecular biologist and therein was a big problem because the way to get this was through molecular biology. And so we had this meeting of a bunch of scientific advisors and I said, well, how can we get a molecular biologist? Who's the brightest, smartest molecular biologist? And they came up with some names and fortunately they came up with George Yancopoulos. Now at this time, the company was really nascent. George Sing, who at the time was at Merrill Lynch Venture Capital, bet on us by putting a million dollars into the company. It was a big bet for George. He got a big chunk of the company for his firm, but he got us started. And believe it or not, George is still with us today on our board of directors. He's a great guy. And so I thought we had all the money in the world, a million bucks, you know, back in 1988 to start a company seemed great. The advisors I was talking to identified Yancopoulos. All we had to do was talk George into joining, which wasn't the easiest thing to do. George wanted to do it, but I had to get past his dad, as it turns out. He was a child of very hard-driving Greek immigrants. And I remember George saying, you know, let's have one more interview between us. I said, okay. I'd already shown them we were going to build these labs how quickly, fast, and you could do an academia. Literally on this campus, we took 10,000 square feet. We now own this entire multi-million square feet campus. We had 10,000 square feet. It was from Union Carbide, who was shrinking immediately post-Bhopal. Anyway, the last interview I came up and George said we needed a restaurant and I couldn't see him in the restaurant. And I saw two people sitting and I realized there was George and his dad. So I had to get past an interview. I was actually being

interviewed rather than the other way around. But at any rate, George joined and the rest, as they say, is history.

Working with Dr. George Yancopoulos

MIKE ROCKEFELLER

You know, that's interesting because looking at your company versus other founder-led companies, you actually have two founders who have been leading this company for 38 years. How has your relationship with George been so successful for so long?

LEONARD SCHLEIFER

Yeah, it's a great question. I'm married for 51 years to my wife, Harriet. And

she's my, I would say, my out-of-work wife. And I like to think of George as my in-work spouse. and the common theme is that in every relationship there has to be a saint. I guess I'm going to argue that I'm the saint in those two relationships that are very long-lasting. Look, from the very beginning, I realized that there were two aspects of building this enterprise. One is sort of the science, the guts of the business, the molecular biology, cloning these things, doing the science, and the other was building the business around the science, funding it, you know, beg borrowing and what have you, they say, to get the money. And I would say we've had a pretty healthy focus where each of us sort of know what we have to do, but we rely on each other for what we do. And so I interact greatly with George on the science. He's a genius, so it's hard for me to keep up, but he interacts a lot with me on the business side. And together, we've managed, because we've had a common purpose. I mean, common background. He's also an MD, PhD. And we knew what we wanted to do. We wanted to use science to make a difference in patients' lives.

Top Moments and the EYLEA Approval

MIKE ROCKEFELLER

Were there any key decisions along the way that really changed the direction of the business?

LEONARD SCHLEIFER

Yeah, there were quite a few. Remember, this is hard to believe, but for the

first 25 years of our existence, we lost money every single year. And I'm not talking nickels or dimes, I'm talking millions and billions. So for 25 years, we lost money. So the key decision we made is despite a lot of people, including the ilks of people like you in the investment community, not you in

particular, but the analysts, the investment community, our shareholders, even our board, you know, pick something, focus, and let's get it across the finish line. And I think that the best decision that George and I made is we weren't going to do that. We weren't going to bet the entire company. It always sounds great, a Hollywood kind of a thing. You bet the entire company on something. Well, if we'd done that, we'd been out of business. We were going to bet on the science, build a foundation of lots of different technologies, and not fall into the trap of trying to bet everything on one molecule. Because we had NT3 and BDNF. George actually cloned the first novel neurotrophic factor since NGF. And we thought we were going to spritz it on patients with Lou Gehrig's disease. We'd cure them. we'd get box seats at Yankee Stadium behind first base and sail off into the sunset in a matter of years. But obviously that didn't happen. But we kept saying, we're going to survive. And when you meet up with a guy like George, it's pretty easy. You know it wasn't a matter of if, it was a matter of when. So I've just viewed my job as making sure we got to that when.

MIKE ROCKEFELLER

What have been your top moments?

LEONARD SCHLEIFER

At Regeneron?

MIKE ROCKEFELLER

Yes.

LEONARD SCHLEIFER

Yeah, my top moments at Regeneron. Well, you know, there were so many, it's hard to recount them. I mean, clearly, just opening up the labs and realizing we were in business was kind of amazing. The IPO in 1991, sort of a big moment. Doing this multimillion dollar deal to really get us going with Sumitomo Chemical, big moment. Treating our first patient with one of our neurotrophic factors, even though it didn't work out, that was sort of a big moment. But the defining moment from a business point of view probably came in 2011. We were sort of heading down the home stretch trying to get EYLEA approved, which we had already approved ARCALYST a few years before, but that was for a very rare disease, although though it's actually selling quite a bit right now. Kiniksa's taken it over and doing a pretty good job there. But we didn't have a significant product that could keep the company going. And, you know, 25 years, people were running out of patience, I think. But in 2011, we knew we had the data. We'd submitted it to the FDA. And sure enough, they gave us in the summertime a CRL. I can't even remember. We've had so many CRLs in recent years and past that it's hard to remember what they felt was missing at the time. I think it was something related to manufacturing again. But my dad at the time was 99 and a half. And he had been driving the car until he was 99 and was in great shape. But he started to go downhill in the

fall of 2011. And we didn't get the drug approved. And he kept saying, "Len, when are you going to get that drug of yours approved?" And right around Thanksgiving, we got the FDA approval. And a few days later, my father passed away. It was almost as though he was hanging on to see that happen. But that was a great moment, a confluence. Not great, obviously, losing my dad, but seeing him, being able to see our success at that age and knowing that we knew we had something. I remember going to the J.P. Morgan, I think it was called the Hambrecht and Quist Conference at the time, in early January 2012. We had just launched the product, and people thought that we were going to sell, I don't know, $5 million. But we sold, like, in the first three months, something like $80 million. And then they thought we were going to sell maybe 100-something the first year, but we sold 800 million. And it seemed like, oh, my God, this is the real deal now. We're a real company. We're treating lots of patients. We're changing people's lives. That was pretty insurmountable times.

MIKE ROCKEFELLER

It's funny. When I was flying out to interview you, I told my kids, I have four young kids, and I said, I'm interviewing the CEO of Regeneron. And they said, oh, you know, who's that? What are they? And I said, well, you know, EYLEA? And they said, no, we don't know EYLEA. Dupixent? No. I said, do you remember when the president got really sick and he got on TV and he said he was feeling better because he took the Regeneron? I said, that's Regeneron. They said, oh, yeah. So that might be their top moment, a small sample size. But that was definitely a top moment.

Treating President Trump for COVID

LEONARD SCHLEIFER

That was an interesting story. I got a call from, I think it was Mark Meadows who originally called, from the chief of staff at the time. And they said they wanted to know. We had just announced, I think on the Tuesday, this was like on a Thursday, just announced that we had some really interesting data that we kind of knew this was going to work. This was a monoclonal cocktail for COVID. And they said that somebody in the White House wanted to get treated. Could we give it to them? I said, it's not the way it works. You can't just give an unapproved drug to somebody, some random person in the White House. You've got to tell me more, and we got to see whether or not the person could qualify for a clinical trial because we were very strict. We just weren't giving it out. We had to participate in our trials. That was the ethical and, frankly, moral thing to do. And finally they admitted that it was the president. And that, of course, changed everything. And I said, look, we can't ask the president of the United States in the middle of a pandemic to participate in a clinical trial, come down to the site on Tuesday and we'll draw your blood and wait. It just didn't make sense. So we had to come up with a way that we could get him the drug. And I told him, the only way that could happen is if the FDA approved it. And we haven't even asked them

about it. They said, don't worry about that. We'll take care of the FDA. I said, well, you say that, but I got to submit it. And they said, that'll all be done within a matter of hours. Seemed like that was done. And I remember them saying, well, when are we going to get the stuff? And I said, well, it was being packaged because it was manufactured in Rensselaer, New York. And we've chartered a plane. And we're going to send that plane down. Well, when's the plane going to get here? When is it going to get there? I said, well, they're going to fly to Dulles. and tell us you got to fly to Reagan. It's much closer. I said, you can't just fly a private jet into Reagan. You know, this is post 9/11. You need 48 hours. You tell your pilot, just head straight to Reagan. What's his tail number? We'll have the military sort of part the way. So I knew this was the serious stuff. And then I had to deal with this wonderful doctor, Sean Conley, who was the White House doctor. I mean, he wasn't equipped to deal with a president who was sick from a pandemic virus. Very nice guy. I had to tell him how you mix it, you hang the IV, you get it in there, blah, blah. And sure enough, we get it into him late Thursday night. At this point, it's been told publicly that given what we know about his condition and the virus, et cetera, that he had a very high probability of dying. And they moved him to Walter Reed shortly after they gave him the infusion in the White House. But it worked like a charm. Within 24 hours, he had turned the corner. And then, you know, sort of our lives changed a little bit because of sort of the publicity, you know, when you save any life, it's important when you save the president of the United States, it became quite the story. But it really did help because there's a real postscript to that. But the bottom line is we were able to save a lot of lives.

EYLEA and EYLEA HD Today

MIKE ROCKEFELLER

And you did it very quickly. You mobilized. It was very impressive.

LEONARD SCHLEIFER

It was really amazing.

MIKE ROCKEFELLER

Yeah. Maybe back in EYLEA. So 2011, it got approved. Most successful

ophthalmology drug in history. You got an approval for the HD. And so for many years, it was an important growth driver for Regeneron. Recently, we've had biosimilars with the 2 milligram. So the franchise has been declining. As you think about the next couple of years, do you see this as sort of a stable business? Do you think there's a path back to growth?

Dupixent and the Type 2 Franchise

LEONARD SCHLEIFER

Yeah, I think there is. I think right now we're at about 50-50 in terms of our dollar sales and HD versus EYLEA itself. As that some of the EYLEA gets eaten up by biosimilars coming along, but some is getting transferred to HD. So I think HD will be able to be a growth in and of itself.

MIKE ROCKEFELLER

And then maybe on Dupixent, your other blockbuster, your IL-4/13, more than a blockbuster, I think it's one of the biggest drugs in the world.

LEONARD SCHLEIFER

It's one of the top drugs in the history of the business. It's the most prescribed drug by dermatologists, pulmonologists, allergists, gastroenterologists in terms of a biologic. It's really, you know, it's taken off because it's a great drug.

MIKE ROCKEFELLER

When did you start working in this area of type 2 diseases?

LEONARD SCHLEIFER

So that was a long time before. George recently showed me some slides. I can't remember how far back, but a long, long time ago. In some respects, before he even came to Regeneron, he had thought about the switch factor and IL-4. And he was an admirer of Bill Paul at the NIH, who had sort of popularized IL-4 as a very important switch factor changing IgG to IgE production. So it's probably a decade or two before that he started thinking about it. Even when it got first approved, we had slides saying all these different conditions we thought that it would get approved in. And then eventually the genetics sort of backed all this up that we had done this all right because you could predict now with our genetic database what indications would work.

MIKE ROCKEFELLER

So you have nine indications.

LEONARD SCHLEIFER

Yeah. I can't even keep track of them.

MIKE ROCKEFELLER

It seems like there's still a lot of penetration left to go in each of the markets that you're in. And I'm sure you're hearing the sell side start to ask questions about the future of the drug. And some of them are saying that they think Dupixent could do over $30 billion in sales by the end of the decade. Do you think that's reasonable?

LEONARD SCHLEIFER

Well, as polite and as friendly and as much as I admire you, Mike, you know that I don't succumb to making predictions about future sales. Because I don't like to make predictions about things that I don't have any more information than you do. You can look at all the same information I have and you can make your best guesses. But I will say this, it's continuing to grow. It's annualizing, I think, based on the last quarter, just the first quarter this year, just under $20 billion. It is not even highly penetrated. I think it's under 20% in atopic dermatitis and less elsewhere. With new entrants, with Lilly's product and other products, you're starting to actually expand a little bit. You're not fighting over the same market share. So we're actually still growing this market. And we're very under penetrated in so many of the indications. I can certainly say I think growth, being a growth driver is an easy bet.

Next Generation Immunology

MIKE ROCKEFELLER

Yeah, I had to try. It does look like it's very possible. You also have some next generation antibodies in the same area. Which ones of those do you think will be most meaningful?

LEONARD SCHLEIFER

Yeah, so once again, we don't try and make singular predictive bets because you start to fall in love with your own predictions. If you think the Mets are going to win or the Knicks are going to win the championship, you start to fall in love with that. And that's okay if you're a fan. But if you're running a business, you don't want to be a fan of your molecules. You want to make sure we bring all of them along and the best will rise. But so what do we have going as possibilities there? I mean, we have with Sanofi, they're looking at how to give more like with hyaluronidase and things like that, how to give more of Dupixent so you can get a greater spacing between doses. we have what we call Supi Dupi which is a long acting version that targets the IL-4 receptor, same target as Dupixent. that's not officially yet in the collaboration but the rules of the road if it's the exact same target we can't develop it on our own and neither could Sanofi so we basically have to discuss if and how and when we put this into the collaboration, but that's coming along, and I'm sure we'll be able to work something out where we bring that forward. We have long-acting IL-13, which we're moving

along extremely rapidly, long-acting IL-4, and we have some bispecifics as well. So we have a whole pipeline of things. We also have new thoughts on, we think we can cure allergy now. That's a bold statement, but I think we can back it up when we get our next generation of molecules, which I hope will be around the end of the year or early next year, into the clinic as a way to knock out IgE cells specifically. I think we've sort of done some proof of principle there already. And so there's a lot for us to go in the type 2 immune space.

MIKE ROCKEFELLER

You put up some interesting data with Lynozyfic and Dupixent in severe food allergy. How come you're not moving forward with that one?

LEONARD SCHLEIFER

Well, we did get a proof of principle there, but we think we have a better one,

a better way of doing this. So the idea there was, let's kill off the immunoglobulin-producing cells. and we used BCMA by CD3 and that killed off all the immunoglobulin-producing cells. The IgG went down, the IgM went down, the IgE went down. And the concept was, well, let's prevent any IgE from coming back by giving something like Dupixent, which it worked. We could get 90-something percent of the IgE gone and it wouldn't come back, but it does take a long time for the IgG to come back. George and the gang had something even better, which could destroy only the IgE-producing cells by some clever trick, which we haven't told the world about yet, which is not so obvious. So I think that rather than spending a whole development program on something where we think a year behind it is something even better, that's the luxury, by the way, of having a long-term perspective. The problem with this business, okay, is that number one, it's hard, and number two, it takes a long time, and number three, it's very expensive. So the very expensive part comes from people like you who pay for all this innovation, because we know the Europeans don't pay for the innovation. We can talk about that. But so if you're going to pay for it, the trouble is your time horizons, maybe not Mike, who's been around for 100 years, but others of your ilk, their timeframes are much shorter. And so the question is, how do you square a circle where the time to do really important things is measured in half decades and decades, yet the time that you guys work in are sometimes milliseconds occasionally or as long as you which some of you consider long term as a minute on the other hand there are some that have been with us since our IPO who really do take a long-term perspective we have we can't if you succumb to those time pressures this is why the you wind up doing wrong the bad things this is why you get so many failures in our industry. It takes time to do things right. And you can't just say, well, I got to have one. If you've got something better, you got to bring that along. So we have either the luxury, the wherewithal, or the foresight, whatever you want to call it, we're going to do things right. And if some take longer than others, that's okay.

MIKE ROCKEFELLER

You have a very deep pipeline of over 50 things that you're trying to get right. So it's really exciting. Maybe to start on the late stage pipeline, because you have some big phase three programs in areas like anticoagulation, multiple myeloma, complement. Which one of those you think is most under appreciated in terms of Regeneron kind of changing the trajectory over the coming years?

Obesity: A GLP That Lowers Cholesterol

LEONARD SCHLEIFER

Well, and obesity, I think you've neglected. This is another big one. You know, once again, how I see the world may not be how you guys see the world. And I don't think we get any credit for our pipeline. Because if you look at what the, if we take your revenue projections for Dupixent, you get all your value back from Dupixent, not to mention the $18 billion we have in the bank. So there is a disconnect that people aren't paying enough attention to the pipeline. Let's start with obesity, just because I think that the way you asked the question, which ones are people ignoring? People are getting a little bit tired of hearing about the next obesity drug that has a little bit more weight loss, or maybe it can be taken a little less frequently, or maybe it's oral. The question is, how do you really change this? And does it make any sense for Regeneron to go in this game? Well, one of the ways to change it, we thought, was to invent a GLP that could actually lower cholesterol at the same time as you lose weight. If you lose 50 pounds on Zepbound or Mounjaro or Wegovy, whatever it is, you barely move the needle on your bad cholesterol. If your LDL was 150 when you started, maybe it's 145. It needs to go from 150 down to 50 or less. And so we wanted to invent a GLP that not only caused weight loss, but lowered cholesterol. And of course, we realized we had one, which was Praluent. And if we could overcome a very hard technical task of getting these together, co-formulated in a volume where you could just give it the same way, you wouldn't even know the Praluent is in there, then effectively we would have a drug that did both. And everybody misunderstands what we're trying to do here. We are not trying to sell more Praluent this way. We can talk about how we're going to sell more Praluent, and we can talk about how Amgen lost an antitrust jury case 400 million to us. We can talk about that market. But that's not what this is really all about. This is about selling a GLP. And because we have a GLP that now lowers your cholesterol. So you can take Lilly's GLP or you can take Novo's GLP or you can take somebody else's. But none of them are going to lower cholesterol. Why not take ours? And I think doctors will like that. And so we get zero credit for that, even though we're well on our way here. We licensed our GLP from Hansoh. So, by the way, in their study, they had much less GI toxicity than tirzepatide did in a similar Chinese study, yet had the same weight loss or more. So the question is, do we think we have at least as good a GLP? Maybe we've got a better one. But when we combine it with

Praluent, we have a total new class of drugs. It's as though we invented a GLP that could also lower cholesterol. So you went to your doctor and you wanted to lose 50 pounds. And they said, by the way, if you lose 50 pounds, you still have to get your cholesterol down. But I have a GLP that does both. Why wouldn't you take that? especially if you could do it in the same injection and hopefully at the same or close to the same price.

MIKE ROCKEFELLER

How hard of a technical challenge is it combining those two?

LEONARD SCHLEIFER

It was not easy, but we've done it.

MIKE ROCKEFELLER

And when can you be in the clinic with that?

LEONARD SCHLEIFER

Well, so we're in the clinic with the GLP. We have to get, the way this works

is that once you get that approved for obesity and for diabetes, then it's easy selling because we're just doing, talking about a combination product. We just have to show that the PK hasn't changed, and it won't. There's no reason. The hard part was doing the proprietary formulation and getting this to work together. That was difficult, and it really had unexpected solutions there. So we own Praluent in the U.S., and we have the proprietary patents on how to combine these things. So that loss is going to go very fast. We're enrolling these trials. They enroll like butter, obesity trials. So I think people are missing that completely.

Lynozyfic in Multiple Myeloma

MIKE ROCKEFELLER

What else are they missing?

LEONARD SCHLEIFER

I think that many have ceded the myeloma space to J&J. They're formidable.

We know them. They're really good at what they do. But at the end of the day in cancer, we think we have a better drug that's maybe more convenient, perhaps less toxicity. We like our data a lot. we're going to commit and this is a 30 or 40 billion dollar space um we're even thinking about monotherapy in frontline so we're very excited you're going to see a ton of work come from us making big commitment that we obviously just recently got approved in the last line we'll get some

data next year in two plus I would think we'll call it then we'll get some data after that in earlier stage, and we've even got data in light-chain amyloidosis, in high-risk smoldering. This is a real big opportunity to simplify and change the paradigm. So that's a big one. I don't think we get much credit because everybody is seated at the J&J. These things can change pretty quickly.

Factor XI Anticoagulation

LEONARD SCHLEIFER

I don't think we're getting credit for our anticoagulants. Okay.

MIKE ROCKEFELLER

That's a big market.

LEONARD SCHLEIFER

That's another $30 or $40 or $50 billion opportunity, especially because the number of people who actually take the DOACs is much lower than who actually should because of the fear of bleeding. And we have two entries there, two antibodies. So like a 1 and 1A, if you will, if you're a horse racing person. You get two horses in the race, not just one with different characteristics. And so we're going to have, I don't know, between half a dozen and a dozen phase 3s going and all sorts of indications by this summer. Some are already underway, whether it's in post-knee replacement, whether it's in cancer, whether it's in DOAC ineligible for atrial fibrillation, DOAC eligible for peripheral disease. I mean, massive big bet there.

MIKE ROCKEFELLER

How are they different from the oral factor 10s that are on the market and the oral factor 11s that are in development?

LEONARD SCHLEIFER

Right. So if you look against the factor 10s, what we see from preclinical data is we can get the same or more anticoagulation, and the genetic supports that with a much lower bleeding risk. The non-catalytic site antibody has really a low propensity. We'll see if it even has an increase. And the other is very mild, but you get better anticoagulation. So once again, the DOACs, they're just not used because of this bleeding problem. In terms of the other factor 11s, if you look preclinically, you'll see that, once again, you know, we just don't make singular bets. We make really good antibodies. We have better anticoagulation and no reason to think we'd have any difference in bleeding than either the small molecules or other antibodies. So, maybe I should pause and point something out. I will say this. I have watched our industry evolve since I got into this business in

1988. You know, you got a lot of value back in 1988 if you had a group of smart people and a prestigious scientific advisory board and an idea. And then this, what I call this sliding lever, moved along in different places. sometimes you had to be you had to have preclinical data then you had to have phase one data say then you had to have proof of concept and and it kept sliding around and and then it's eventually what you got to have be in phase three to get value then of course people realize well maybe you got to have a successful phase three then oh my god you got to get past the FDA and then you got to get it to be commercial, and then you got to get past the payers who are really difficult and the Europeans who I call the non-payers. And then you got to worry about competition now from China and everywhere else. The world has changed. We had a massive head start on Dupixent compared to the rest of the world. EYLEA, people have been chasing EYLEA for 10 years. No one's been able to come up, 15 years. No one's been able to beat EYLEA. But I think those days are sort of numbered, numbered in the sense that you won't have the kind of lead that you might have had if you come up with something out of the box, because people catch up now so quickly. The tools are out there. So we like to do two things. One is we like to have a lot going on. So instead of one $20 billion product, maybe we have four, five, $5 billion products at a time where it's easy to be more predictive. And who can do that? Only people who can put 50 things in the clinic with another half a dozen or more every year going into the clinic. So we think that that strategy of doing as much as you can broadly and accepting the fact that you'll have competition sooner is probably the best strategy that works. Now, that's, of course, very self-serving, Mike, because nobody else does research like George and his team. So I think that we have a competitive advantage now in this new marketplace where building a company on one single blockbuster like a KEYTRUDA or Mounjaro or Dupixent is going to get harder.

The C5 Franchise

MIKE ROCKEFELLER

Yeah. It does seem like you are getting more credit for your C5 franchise and MG and PNH, but you've also put up great data there.

LEONARD SCHLEIFER

Yeah, I forgot to mention that. That's it. That's the beauty of having so many

things. Our C5 franchise, I think, has got the best-in-class data. We've shown that for PNH, you really need to push the limits a little further than just the antibody alone. So the antibody plus the siRNA we've shown can really take people who are not fully controlled by looking at their LDH, for example, which is a measure of intravascular hemolysis. We've shown that you can do better. So we're waiting for the final data on that. But we've already shown in myasthenia gravis, you don't

need all that. And just the siRNA alone, which can be given quarterly and get the same kind of data, that's going to be, I think, a very competitive in a marketplace that's really growing.

MIKE ROCKEFELLER

The one area that we haven't seen data for that franchise is in geographic atrophy.

LEONARD SCHLEIFER

Yep.

MIKE ROCKEFELLER

Million patients in the U.S., so a lot of opportunity.

LEONARD SCHLEIFER

Big opportunity there. That's more speculative, I would say, but we have to do the experiment because they've shown that you work intravitrally. we think most of the C5A comes from the liver. So you want to block this systemically. But we also have a plan to block it intravitrally as well with a better, cleaner antibody that's not pegylated and going to have some of these immune problems. So the reason these drugs haven't taken off is because they have these toxicities of these occlusive vasculitis. And they may cause wet AMD to boot. So it's not been a clean class or they would have done a lot better I think because even though it's only at 20, 25 slowing that's pretty important if you can do that safely because you just don't want to have your the retina to atrophy I mean it's a big issue so anything you can do to slow that down safely is a winner so we'll see there once again you know these are bets we'll make we don't bet companies on these things, but we have so many different ways to win. We have some really cool stuff we haven't talked about. I think we're going to turn the world a little bit upside down in some of fatty liver disease. Our genetics has given us approaches and ideas that are just, I think, going to sort of maybe revolutionize that space a little bit. We've got a genetics target that's given us a great leg up on glaucoma. We're looking at that. We've got another genetic based target, which we're starting very soon on Sjogren's disease and several other of these fibrotic type immunologic diseases. I mean, it just keeps going and going.

The Regeneron Genetics Center

LEONARD SCHLEIFER

And we haven't even talked about our Regeneron Genetics Center, which has got the largest collection of data, which is extremely interesting. And we've been struggling, but we're trying to come up with an idea. We've been struggling how to take a real advantage outside. I mean, we use it every day for discovering and developing drugs, validating pathways, all that. But we think

there's a health tech business there too that we can, because, you know, we have one of the largest databases in the world where you link genomics and soon proteomics. and with electronic medical records, and with all the AI companies. I think it's going to be very interesting how we can do this. Some cool stuff, by the way, you can do with proteomics. If we took your blood, we could tell you how old you are. Now, I could pick your pocket and look on your driver's license so that it's not that big of a deal, but we could do it from your blood. But we could also tell you not only how when you were born, we can tell you how you've aged. So you might be 40-something, but you might be 60-something because you haven't treated your body right or genetics are not so good. Or you could be 20-something. So you can find very interesting correlations between what's going on in your blood and what's going on in your genome. So, for example, you might be at very high risk for Alzheimer's disease. but we can tell you whether or not you are, despite this high genetic risk, whether you have a 100% chance or a 0% chance of actually getting the disease by looking at your blood. There's so many powerful things we're beginning to realize when we start to study genomics, proteomics, and electronic health medical records. So trying to figure that one out too. You know, we do a lot. We're ambitious, but there's so much to do, so it's exciting.

MIKE ROCKEFELLER

Yeah. You mentioned liver disease, and as I was going through your pipeline, you have a couple phase two assets for MASH.

LEONARD SCHLEIFER

Yeah.

MIKE ROCKEFELLER

Which ones are you most excited about?

LEONARD SCHLEIFER

The ones I haven't told you about. Stay tuned.

MIKE ROCKEFELLER

The leading MASH company, Madrigal, just in-licensed a PNPLA-3 for MASH from Arrowhead. And you have one as well in phase two. Is this an interesting target?

LEONARD SCHLEIFER

Yeah, it is an interesting target, particularly for those who have this fairly common mutation. We know Bill Sibold, by the way, quite well. We like Bill. We know him from his days at Sanofi where we work with him. And he seems to have done a good job. You know, nothing lasts forever, Bill. We're coming after you.

MIKE ROCKEFELLER

You're known for pioneering human monoclonal antibodies. That's, you know, I mean, you do it better than anyone.

LEONARD SCHLEIFER

I would say George is known for that.

MIKE ROCKEFELLER

George is known for that.

LEONARD SCHLEIFER

He does it better than anyone.

MIKE ROCKEFELLER

Give you some credit also.

LEONARD SCHLEIFER

Yeah.

MIKE ROCKEFELLER

Interestingly, when you look at your pipeline now, a quarter of it is in siRNAs.

LEONARD SCHLEIFER

Yes.

MIKE ROCKEFELLER

What is special about that modality that is a quarter of the Regeneron pipeline?

LEONARD SCHLEIFER

Yeah, there are just, you know, targets. Well, let me back up. First of all, we love platforms. Monoclonal antibodies is a platform. siRNA is a platform. Gene editing is a platform. And there were other platforms coming along that we're very interested in. The main attraction of siRNA is its ability to address targets that are not otherwise draggable easily, let's say, by a monoclonal antibody or even a small molecule. So that's what's particularly. I think people do tend to misuse technologies. You know, TTR is a good place to use it. Putting an siRNA in the eye to try and lower VEGF would be a dumb thing to do. But there are places where you really can't get to targets where siRNA can get you there. And we've been working with Alnylam on some CNS targets, which are very interesting. I can never remember which ones we've told you about, which

ones we haven't, so I won't get myself in trouble. But that's the main advantage. You can quickly try and address targets. And, of course, they remarkably, and nobody would have believed it, have this incredible long half-life that they can work.

MIKE ROCKEFELLER

Anything in the early pipeline that we should be asking you about?

LEONARD SCHLEIFER

You know I won't get much credit so why bother to educate the rest of the world

I think I threw one at you glaucoma the uh fibrotic immunologic diseases Sjogren's and others that's a very interesting one I told you that we got something really interesting in the the MASH world, we got a lot I mean we put half a dozen or more every year into the clinic and 50 in the clinic so.

Curing Genetic Deafness

MIKE ROCKEFELLER

It was amazing seeing that child at the White House.

LEONARD SCHLEIFER

Really amazing.

MIKE ROCKEFELLER

Yeah.

AI in Drug Discovery

MIKE ROCKEFELLER

You had talked about Regeneron's Genetic Center, and you're a leader in technology and data. How are you using artificial intelligence right now in your R&D?

LEONARD SCHLEIFER

Yeah, so two ways. One is the obvious way that any business could use. If

you've got to write a protocol that's this thick, well, AI can write a first draft of that in a minute. Rather than have somebody prepare me for Rockefeller's hard questions, I can ask AI to do it. But that kind of what I call, quote, unquote, busy work is what AI is particularly good at. But if you know how AI

works, and I've got a real lesson from this from George because he thinks about this stuff and he really, this all is intuitive to him. I have to think on it hard. But, you know, it's not really thinking. It's statistically putting things together just based on what it's trained on but and you know it might come up with a a new drug based on a small molecule scaffold or something but do we need it to design an antibody hell no we got our humanized mouse makes human molecule antibodies by the thousands and in fact the AI people all came to us wanting to get access to our collection of structures and antibodies so they can train. I mean, so we don't use it to discover the actual drugs, but we use AI in our genetics to find the right correlations, what's the right relationship, and it can do some of these big data tests faster and more powerfully than old methods could do that.

MIKE ROCKEFELLER

Do you see that evolving over the next several months or years?

LEONARD SCHLEIFER

Yeah, I think that we're looking about how to take advantage of AI and our data set, these millions of people, and see if we can't get more into the management of health care, not just by drugs.

M&A; Philosophy

MIKE ROCKEFELLER

Interesting. M&A. So you've taken, I would say, a different approach versus

a lot of your peers, which is just focusing on technologies and platforms, as you mentioned, often early stage, smaller deals. Do you see that strategy evolving as the company continues to scale and grow over the coming years?

LEONARD SCHLEIFER

Yeah, it's a good question, Mike. I don't think our strategy will evolve

because I don't think it has devolved or it's never really changed. We are interested in any and all opportunities. We prefer things that are platforms. We prefer working with people who are like-minded and want to work with us where we can be additive together and one and one can literally make three. We want to make money and what we do um this notion that that this is free because you're taking it from your balance sheet and you can non-GAAP it or do something all that to us is so maybe a driving factor people talk about their M&A capacity you know, I don't think of that as a proven strategy destroy value you show me companies that have done that well. You know the one that's done it the best? Once, which is Sanofi with Dupixent. And they'll admit that. That was a great partnering kind of a thing. But competing for late stage or approved assets, there's not much to that because you're spending $10 to turn it into $6 frequently. And that's because people are so

desperate. We literally have seen things that we thought were worth just to pick an arbitrary number, six, and people willing to pay 12. That's just crazy for us, especially because we have such a rich pipeline of our own. So if there was a great asset, I mean, we've got $17, $18 billion in the bank and we've got a lot of capacity. If there was a great asset that we saw value in that others didn't, Yeah, we would do it. We're not constrained by size. People don't really understand how all this works. We don't tell Nouhad Husseini, who is a great head of BD, hey, this is what you can spend this year, go out and spend it, and we're desperate for a phase three or something like that. We just look at the whole universe of things and what makes sense for us. And I just think it's a far more rational way of doing that. To me, you should view all this as one. That is, our goal as a company is to get products that make a difference to people, and that will help people and it will help our shareholders. If it comes to my research, which is most likely for us, that's more efficient, more predictable. But if we have to go outside, we have no problem with that.

MIKE ROCKEFELLER

So could a large deal or even a merger ever make sense for a company like Regeneron?

LEONARD SCHLEIFER

Sure, but it'd have to be value creating. And that's the hard part, why it's unlikely, but it'll have to be something that we see that's not visible to others at a price that makes sense compared to what others are willing to pay. And we've been involved in some of these mid-sized kind of discussions, but everybody pays these crazy numbers. It doesn't make any sense.

Succession and Advice for the Next Len

MIKE ROCKEFELLER

So you've been leading this company for almost 40 years. what does the next chapter look like for you personally and for the company whenever that time comes so that you can ensure that Regeneron and its culture endures?

LEONARD SCHLEIFER

Yeah. You know, founder-led companies really, Mike, are different. George and I have been leading this company for a long time, and it is our life's professional work. We do this 24/7. We slightly keep different hours. So when I'm at home, George is maybe still in the lab or coming home. He's calling me or I'm calling him when he hasn't. And we're talking all the time and we're loving what we're doing because we were just so excited about the prospects of it's like living the dream of making a difference in people's lives and in doing that in a productive way with the appropriate financial rewards. I think it's great. But no man lived forever. And so we are developing talent on a constant basis. I want to do it. I know George wants to do it as long as we feel we can be the best people to be in the job that we're in. And when we're not, we have a deep bench of people that I think can take our place. But I like to think that there's a way about doing things, there's an ethical approach, there's a patient-first approach. I mean, I hear about some of these companies that, you know, I won't use names of people who the FDA wants to withdraw a drug because the data was manipulated according to the FDA and there's safety concerns. And they're still fighting whether or not to take it off the market. It's like they're in the widget business to me. I mean, they must have their own perspective on these things. But there are companies like that. That's not who we are. We like what we're doing. I think we're still doing it well. I don't think that people fully appreciate the difference the way a founder-led company is managed versus the, what I, you know, we're not renters, we're owners, so to speak. You know, you have a CEO or a CSO, they normally have, what, a five-year horizon or something like that. You know how many CEOs I've worked with at Sanofi, by the way?

MIKE ROCKEFELLER

How many?

LEONARD SCHLEIFER

Eight. Eight.

MIKE ROCKEFELLER

Wow.

LEONARD SCHLEIFER

So you know that's not who we are and so we like the what we do and we think we're good at it and we want to keep going but as I said we'll know when it's time to let the young bucks take over.

MIKE ROCKEFELLER

You've done an incredible job. Before I let you go what advice would you give to the next Len who is thinking about leaving the lab and starting a company?

LEONARD SCHLEIFER

Well I think the first thing I would do was find a George. That may be

impossible because they probably broke that mold. But in terms of general advice, I would have to say you've got to have the right, the long-term perspective. Do not make singular bets. Ignore all the stuff that you hear from the analysts. I used to get in my early days, and sometimes I still do it because I can't resist a good fight, but some of the analysts who have these crazy views of Regeneron. You've just got to ignore all that noise. Even the shareholders, you can't ignore them, but you have to educate them that we're not here to make you money this quarter. You want to bet on whether or not when we turn over a trial, that's your business and that's okay, and you can make that wager with any ways that you guys can make those wagers. But I would say to somebody focus on the long term, focus on the science, focus on what you're really trying to do is make a difference to patients. You really are not in the widget business and have a really strong moral compass. There are going to be some down times where you've got to be willing to say this is not right I'm not going to do this and you've got to resist all those pressures.

MIKE ROCKEFELLER

Great advice. Thank you for all you've done for patients and for shareholders, Len. Appreciate the time.

LEONARD SCHLEIFER

Thank you, Mike. It's been a pleasure knowing you. You've been doing this for decades, but you don't look like you've changed. So kudos to you.

MIKE ROCKEFELLER

Maybe we have a couple more years left in us.

LEONARD SCHLEIFER

Yeah, I hope so. Great to see you.

MIKE ROCKEFELLER

Thank you.