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EDITED TRANSCRIPT

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OVERVIEW:

Company Summary

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PRESENTATION

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Good afternoon, everybody. I'm Chris Schott from JPMorgan, and it's my pleasure to be introducing Regeneron today. From the company, we're going to have presentations from Co-Founders and Co-Chairs, President and CEO, Len Schleifer; as well as President and CSO, George Yancopoulos.

2023 was obviously a very successful year for the company, significant progress across both the core drivers as well as the pipeline and looking forward to the update from the team today on the business for '24 and beyond. So with that, turn it over to Len.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Thank you, Chris. It's great to be here. Let me start with a very important piece of business. I think as everybody knows and we announced several months ago, our spectacular CFO, Bob Landry, will be moving on to greener pastures. So Bob, thank you very much for leaving us in such a great shape, and we welcome Chris Fenimore, who will be taking over after Bob signs the 10-K. Somehow it seems like Bob is on a mission to get the stock price so high that we appreciate his value. But we do anyway, Bob.

Second minor order of business is that today happens to be our birthday, not my birthday, the company's birthday, January 8. So happy birthday to all of us at Regeneron.

And the last piece of small business is to go through every line of this forward-looking statement slide. Please look at it carefully. We're going to make a bunch of forward-looking statements. They might not all come to pass, and you should look at our filings and our website and so forth to understand the various risks associated with that.

So, turning to 2023. 2023 was a pretty important year for us. We had a lot of strategic things that needed to get done. And the top 2, I think, on the list had to do with EYLEA and DUPIXENT, our most important commercial products. And fortunately, after a tiny bit of rock and roll, if you will, we managed to get EYLEA HD launched in August, and I think that puts us in a very strong position for a prolonged leadership in that space. And I'll get into that in a little bit more detail.

We also needed to win with our partner, Sanofi, on our COPD data, and that turned up also quite spectacularly. And we'll tell you a little bit more about that as well.

And then finally, the big other strategic imperative for us was to make sure we kept focusing on the pipeline. Inside the company, it's very easy to look at today's sales and so on, but we really have to always -- we're a business about the future. And there's been some incredibly exciting developments in the pipeline that George is going to tell you about in just a few minutes. And he'll touch on just a little bit on the things that we have, over 3 dozen -- I think about 3 dozen molecules in development and many more in preclinical development spanning many different areas of drug targets.

Sometimes it's good to look back. If we got a lot done, we'll show this slide. If we didn't, we kind of skip it, but we did get a lot done. This is what we told you we were going to do a year ago at this conference. You can see a lot of checkmarks. We missed on a few things, but by and large, we got what we said we would get done and what we work very hard at and frankly, a lot more. A lot more had to do with many things we didn't even talk about last year, which were in the pipeline, which, as I said, George will get to in just a minute.

EYLEA HD, very important for us. We have -- we're off to a very successful launch, $123 million in the first quarter. That is really quite a good achievement by all measures compared to other recent launches in the space, compared to our own data on EYLEA. This is really good. And it occurred despite the fact that there's still fair amount of prescriber hesitancy related to the fact that we don't have permanent J-code. So some people are actually concerned about reimbursement, but this went really well for the first full quarter. And I think that the early indicators are suggesting broad uptake from all sorts of patients, converting EYLEA 2mg patients, converting other branded drugs and even naive patients.
It all stems from the data. We had great 2-year data, which you're all, I think, very familiar with.

We have a lot of -- despite the hesitancy, we do have a lot of covered lives. About 2/3 of lives are covered. But the J-code should help, and that's coming, we hope, around the beginning of April. So EYLEA HD, off to a very good start.

DUPIXENT is the product that just keeps doing wonderful things for so many different patients. It's something that we do in close collaboration with our friends and colleagues at Sanofi. Together, we've been on a remarkable journey. When you measure it in terms of actual dollar performance in the first 3 quarters of the year, growth was about 34%. And it reached nearly $8.4 billion in the first 9 months of the year, more than 3/4 of a million patients on the drug. It's been approved in 5 indications. There's positive pivotal results so far in 7 different types of Type 2 allergic diseases. We're #1 in new brand in all our approved indications -- new to brand and we'll probably be soon to be #1 in total Rx in all of our indications.

The safety profile is really quite remarkable for a biologic, and George will get into some of the reasons for that. But I think also you're going to hear some really exciting data how DUPIXENT might be used to cure allergic diseases. So this is a product that keeps giving. This is sort of the journey we've been on with Sanofi from its first approval.

And just to highlight, if you look carefully at this, you'll see approvals for as young as 6 months. The FDA, doctors... you don't approve a drug for babies unless the safety is really terrific, and the efficacy is outstanding. And I think that that's what you see with DUPIXENT.

You can see where we are today. We still have many more to do... important next part of the year to launch, we hope, for COPD. Sanofi and Regeneron are preparing for that launch. There's a lot of patients who we need there. There's probably 0.5 million patients in the G7 that would meet the criteria that we hope to be able to get in our indication statement. So DUPIXENT is the product -- truly the product in a pipeline, it's going extremely well.

In oncology, we've set out an internal goal for us to be a leading company by the end of the decade. That is, I think, on a good trajectory for that. We have lots going on with our anchor to that program, LIBTAYO, but we've managed to file both with odronextamab, our CD20xCD3 bispecific and our BCMAxCD3 bispecific in advanced multiple myeloma patients. Both were filed by the end of year. I should have mentioned it, so was the COPD for DUPIXENT. So the regulatory groups were very, very busy, but we got a lot done. But we think this foundation that's been -- that George and the team have been laying, where we have validated 3 different classes of immuno-modulary agents in cancer, sets us up very well for success.

So what I'd like to do is just conclude there at this point and say pay very close attention to some of the things George is going to talk to you about. I personally have a favorite, which is his ability maybe to cure allergy, but you guys may have a different thing. There are so many great things going on. I'm going to leave it for George to tell you what his favorite is.

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

Thank you, Len. As you heard, today is our birthday. And when we started the company 36 years ago today, I was still in high school by the way, but we very quickly became known for our scientific innovation. And one of the things that I'm proudest of is that, after all these years, we continue to relentlessly push the boundaries of science and technology.

And so, 2023 was yet another year of firsts for the industry and the world delivered by Regeneron, with several having the potential to change the practice of medicine: from developing the first biologic to achieve clinically meaningful benefit in COPD; to pioneering a series of novel combinations in oncology and genetic medicines; to using CRISPR and siRNA to silence pathological genes; to inventing a gene therapy to restore hearing in profoundly deaf child; to developing an approach to potentially reverse severe allergy, that's what Len is very excited about. All of this represents our commitment to continually, relentlessly invent and develop new technology that can benefit patients' lives.

So today, I will review some of the highlights of our expanding pipeline, which are all representative and coming from this commitment we have to relentless innovation. Before I dive into the oncology pipeline, I'd like to describe our overall oncology strategy, which is primarily focused on using the body's immune system to fight back against cancer. And we have clinically validated, as Len just told you, 3 independent classes of internally developed immuno-oncology agents with each class modulating the immune system in a different way and able to be used in combination with one another to potentially augment antitumor activity.

Our checkpoint inhibitors, including our PD-1 antibody known as LIBTAYO or cemiplimab; our LAG-3 antibody, fianlimab, are designed to overcome T cell suppression, thereby empowering T cells to kill tumors. Our CD3 bispecific platform bridges T cells to tumors, so the T cells can kill the tumor cells. And we have a very large pipeline of CD3 bispecs each specific for different tumors with our first 2 currently under FDA review. And I remind you that Regeneron was the first to put CD3 bispecific antibodies into human trials.

And finally, our CD28 co-stimulatory bispecific platform, which currently has 4 programs in the clinic and many more soon to enter, designed to enhance antitumor activity of either the first class, the checkpoint inhibitors, or the CD3 bispecifics. And I want to also point out that we introduced this therapeutic class to the world as well.

It's the unique flexibility that we have that I think really distinguishes our program. Our immuno-oncology efforts were prospectively designed so that the various individual agents I just introduced to you could be combined in logically intelligent ways to optimize and tailor the right combination for the right tumor type, resulting in a very broad and multifaceted portfolio of combinations.

And this slide highlights 1 such combination of 2 of our checkpoint inhibitors, cemiplimab with fianlimab. Ever since the exciting early data with individual checkpoint inhibitors more than a decade ago, it's been everybody's dream that combining 2 classes of such inhibitors might meaningfully enhance anticancer benefit without exacerbating safety issues. Our early clinical data, as summarized on this slide with cemiplimab and fianlimab in melanoma suggests that this combination might be the first such example of really truly additive benefit without exacerbating safety. We're hoping to deliver potentially pivotal data from our ongoing first-line metastatic melanoma trial by the end of this year.

Moving to the recent progress we've made with our CD3 bispecifics. Recently at ASH as well as in recent press releases, we updated data for both odronextamab in late-stage lymphoma patients and linvoseltamab in late-stage myeloma patients, with both programs currently under review by the FDA. To focus on one of these, the linvoseltamab data is compelling compared to the 2 other recently FDA-approved BCMA bispecifics. Most notably, with similar amounts of follow-up, linvoseltamab shows much higher rates of complete responses in these previously relapsed and refractory patients with a favorable safety profile and potentially shorter hospitalization requirement as well as the opportunity for more convenient monthly dosing.

In summary, with its differentiated efficacy, safety and convenience profile, linvoseltamab is poised to be a competitive agent in late-stage myeloma and a great foundational agent to be explored in earlier lines of therapy as well as in innovative combinations.

And in terms of such innovative combinations, I want to next discuss our CD28 costimulatory bispecifics. Last year, we presented unprecedented antitumor activity in late-line prostate cancer with our combination of our prostate-specific costim bispec with cemiplimab. But unfortunately, the responders tended to have serious associated immune-mediated adverse events.

We continue to work on mitigating this toxicity and plan to soon investigate combinations of our prostate-specific costim with prostate-specific CD3 bispecifics, which we believe will be better tolerated. We are currently exploring multiple additional CD28 costim bispecifics in early clinical trials across a variety of tumor settings, in combination with cemiplimab or with corresponding CD3 bispecifics.

Importantly, we have not observed a similar toxicity profile in our other CD28 costimulatory programs that target different tumors and different tumor antigens. And importantly, for the 2 CD3 bispecs in lymphoma and myeloma that I just reviewed, we are very excited about progressing combinations with corresponding costim bispecifics for each, which hopefully will extend the activity in their settings.

Now shifting from cancer to immunology and inflammation and in particular, to COPD. Following the unprecedented results in eosinophilic COPD that we reported with DUPIXENT from our first Phase III trial, BOREAS, we recently reported that our second Phase III trial NOTUS confirmed these results.

These studies represent the first time that a biologic was able to achieve clinically meaningful [reductions] in exacerbations and also improve lung function. Our sBLA in conjunction with Sanofi was submitted in December, and we are preparing for potential launch as early as midyear. As reviewed by Len, this would be the sixth potential indication for DUPIXENT and the fifth for which it would be first in class.

Itepekimab, our IL-33 antibody, also has the potential to transform the treatment paradigm for COPD but for a distinct subset of COPD patients. The AERIFY Phase III pivotal trials were designed based on our Phase II data and compelling genetics data from our Regeneron Genetics Center and are evaluating former smokers with COPD regardless of eosinophilic phenotype. Last year, the AERIFY studies passed an interim futility analysis, and we remain on track to read out pivotal data from these studies next year.

Now, many of us think DUPIXENT is pretty amazing in terms of its ability to provide [meaningful] clinical benefit across so many so-called allergic or atopic diseases. But what could be the next big opportunity for Dupi? Since Dupi worked so well in so many allergy-related diseases, could Dupi directly benefit severe allergies?

As many of you know, allergy is due to pathologically high levels of the IgE class of immunoglobulins. Because of this, some people say that the E in IgE stands for Evil. Early on in our Dupi efforts, we realized that patients treated with Dupi no longer made any new IgE, but they continue to make the IgE that they had already been making. That's because Dupi blocks what is called class switching to IgE, but it doesn't eliminate the existing long-lived plasma cells that have already switched to IgE. So Dupi by itself prevents new allergies, but it doesn't reverse existing allergies.

Relevant to this, we made an astounding discovery with our BCMA bispecific for myeloma. Remember, myeloma are cancers of the immunoglobulin producing plasma cells. In addition to killing the malignant [myeloma] , our BCMA bispecific also naturally killed the nonmalignant plasma cells in these patients, including the preexisting long-lived IgE plasma cells in these patients, reflected by a rapid drop in IgE as seen on the slide on the lower right. So in humans, we know that BCMA essentially eliminates IgE. The problem is as soon as you stop treating with the BCMA, the IgE levels come back.

The above insights, combined with what we observed with Dupi, suggested a novel combination approach that might eliminate allergies as we recently confirmed and described in nonhuman primates in a high-profile publication featured on the cover of Science Translational Medicine. The middle panels show this data that, as seen in humans with the agents individually, a single dose of BCMA bispecific immediately drops IgE. But when you stop the bispec, the IgE comes back, but also as predicted from how Dupi behaves in humans, it does the same thing in animals. If you add Dupi after the single dose of BCMA, it permanently eliminates IgE.

Notably, this approach allows repopulation of cells that produce all the other immunoglobulin classes, which is why we believe this approach could safely potentially reverse severe allergies. Based on the observed individual actions of Dupi and our BCMA bispecific on IgE in humans, and these existing combination data in nonhuman primates, we plan to initiate a clinic trial this year to see whether this combination can safely and effectively reverse severe allergies, and particularly food allergies. That's why Len is so excited about this.

Okay. So moving on to obesity, where we have several early programs. As everyone knows, GLP-1-based therapeutics such as semaglutide have transformed the management of obesity, delivering significant weight reduction along with improved cardiovascular outcomes and glycemic control. However, there is increasing recognition that the quality of weight loss from these medicines is suboptimal with up to 40% of the weight loss due to loss in muscle. So for example, if you're an older obese patient who loses 30 pounds, which is not unusual, you will lose up to 12 pounds of muscle. You'll never get it back. The problem is when patients go off this drug, as the vast majority do within a year, they rapidly regain their weight as fat. This is potentially going to lead to a massive public health problem.

We have clinically validated antibodies that can address this problem in that, in humans, we have shown that they can preserve and grow muscle. And as shown on this slide, once again, in nonhuman primate studies, we combined what we knew they already did in the setting of combination with semaglutide to show that they can indeed improve the quality of weight loss, resulting in actually more fat loss, while either saving the muscle or actually growing the muscle during this period of caloric restriction. So pretty exciting, incredible data and opportunity, and we'll be initiating our trial this year to test these muscle preservation agents in combination with semaglutide.

As I mentioned, we're also leveraging our capability in genetics in the obesity space, highlighted by the discovery of the GPR75 target by our Regeneron Genetics Center. This target may provide for an entirely new mechanism to fight obesity. In early data with our siRNA lead that we're developing together with Alnylam, silencing GPR75 shows impressive activity in preclinical models, completely blocking body weight gain and fat gain, while leaving lean mass unchanged, primarily acting through increase of physical activity in both mice and humans.

Following up on the GPR75 story, let me move on to our additional efforts in genetic medicines. We have established clinical proof of concept across several diseases using multiple genetic modalities. Our collaboration with Alnylam using siRNA has achieved proof of concept for silencing genes in the liver and in the brain for the first time in human history. For CRISPR gene editing, our collaboration with Intellia continues to advance, now with the lead program for TTR cardiomyopathy entering Phase III, the first CRISPR program to be entering Phase III; and our first gene insertion program entering the clinic soon to potentially cure hemophilia B and; finally, our AAV gene therapy efforts, including our efforts in genetic hearing loss as well as our continued efforts to use antibodies to better target genetic medicine payloads. And this slide depicts our growing genetic medicines pipeline.

One increasingly important approach for our pipeline is combining to siRNA with antibodies. Our C5 program is the first-ever combination of combining an siRNA with an antibody for a specific target. The siRNA markedly decreases target load, C5 production by the liver, allowing much lower levels of antibody to be used to completely block the residual C5, which we hope could provide better efficacy and control of breakthrough hemolysis in patients with PNH with much more convenient dosing.

And that's exactly what we achieved in the clinic. As we recently reported for an exploratory cohort from our ongoing Phase III trial with this combination, patients treated with this combination achieved greater control of intravascular hemolysis compared to the current standard of care, and we were able, for the first time, to drive LDH levels to normal levels in PNH patients.

Building upon this encouraging C5 data in PNH, we are rapidly extending this combination approach to geographic atrophy in dry AMD with 2 Phase III trials beginning this year. Recently approved approaches inhibiting complement are approved for slowing progression of geographic atrophy, but must be delivered directly into the eye and come with risk of severe eye inflammation and even blindness. We believe that our systemic approach has several significant advantages over these recently approved agents.

Finally, I would like to highlight our first gene therapy program for genetic hearing loss. Today, we update results for our first treated child who was born completely deaf and was still deaf at baseline. Our gene therapy treatment improved this child's hearing test at 4 weeks, and we now report that the child's hearing has continued to improve. At 12 weeks, tests now show that the child has remarkably improved to the moderate hearing loss range. We are very excited by these nearly miraculous early results for our innovative approach for this ultra-rare genetic form of hearing loss and believe it bodes well for our upcoming efforts in more common forms of genetic hearing loss.

Now, a major limitation of genetic medicines is delivery to cells of interest in the body. Currently, systemic delivery is largely limited to the liver targets. And as I just showed you in the case of the ear gene therapy, it requires local surgical injection to deliver the AAV to that position. We have been long now working on and developed a proprietary approach that leverages our antibody capabilities to be bound to and be used to target and deliver genetic payloads to specific cells in the body, an approach we have now validated in nonhuman primates and which we believe addresses the real bottleneck for most genetic medicines efforts outside the liver, i.e., delivery.

This slide lists the anticipated 2024 milestones, and I hope we do as well on these as Len showed that we did for 2023. And we're already off to a great start with Bayer's announcement today that aflibercept 8 milligram was approved in Europe.

I will close with something core to our company. Since our founding, Regeneron's mantra has been doing well by doing good. While this starts with our efforts to bring life-changing medicines to patients, we believe in being good corporate citizens. One important way is by trying to inspire and engage the next generation of scientists. And in part, we do this by being the primary sponsor of the nation's major high school science fairs and competitions.

As both Len and I got our start in these very science competitions, I find it astounding that they now bear the Regeneron name. So with that, I'd like to thank everyone for their attention, and let's head to Q&A.

QUESTIONS AND ANSWERS

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Appreciate the comments. Maybe I'll just kick off with just some comments on -- or some questions on EYLEA HD. So maybe just elaborate a little bit on the launch so far. So how are general trends playing out versus your expectations? And maybe just a little bit more detail in terms of the characteristics of the patients you're seeing who are starting on therapy there?

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Marion will take that question, but I just -- before she does, I just want to clarify, so we don't mislead anybody. George and I both participated in the -- what was known as the Westinghouse Science Talent Search. George was a winner. I was just a semifinalist, hence, our roles. Marion can cover that question now.

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

I certainly will. I hope my mic is working. Great. Okay. So on EYLEA HD, we're really pleased to give you the results today on our fourth quarter performance. We launched, of course, in late August. Characterization of launch of EYLEA HD has been very positive. The early response we've had from physicians on enthusiasm based on clinical data was very, very strong as you know. And now that has translated into patient experience, which has been very positive in terms of the feedback. Basically, in summary for EYLEA HD combining the efficacy that we've seen now with EYLEA as the standard of care, safety that is paramount in this category and then beyond that, the durability that has been the gap in care.

So early days, very positive. Some unique characteristics would be, with EYLEA HD, we're seeing physician experience, early days, with understandably recalcitrant patients but also with patients being switched from EYLEA or another branded product because they're looking for greater durability. And as well, we are getting initiation in therapy with EYLEA HD from patients on Avastin that aren't getting the response needed and then even in some cases, less frequently, but in some cases, naive patients.

So strong start, as Len mentioned. Reimbursement is tracking with our goals, actually ahead of goals for reimbursement coverage. But having a permanent J-code will be important come that April 1 time frame in terms of giving additional reimbursement confidence.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Can you elaborate a little bit on the J-code? In terms of your interactions so far, [for] what percent of practices is the lack of a permanent J-code a hurdle in terms of adoption?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Chris, it would be hard to give you a percentage. I would only be guessing, but what I'll say is that we now have, on a national basis, certain practices, individual prescribers, but even large group practices that are holistically adopting use of EYLEA HD. There's somewhere -- it's more of a mid-response, some practitioners moving forward. And then you always, with a launch, will have some that want to wait a little bit, wait and see.

But then if you ask me the question what would be the #1 characteristic that people want to see more of, it's not any lack of assuredness on EYLEA. As they often say, EYLEA HD is EYLEA made better. It's not the clinical profile. It's not safety. Everybody wants greater durability. It's not hard to understand that people don't want more frequent injections in their eye. So I think the #1 thing would be confidence in reimbursement, which is, to some extent, a by-product of having more new agents in the category recently and perhaps sometimes not having the reimbursement they'd hoped for.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Yes. Okay. Great. And then just on competitive dynamics, how has the conversation changed, I guess, with the HD launch as you think about the broader competitive landscape?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

I think now we have the opportunity. EYLEA has been the standard of care. And now with EYLEA HD, we meaningfully have the opportunity to become the next standard of care in the anti-VEGF category because we provide everything that's been near and dear on EYLEA. Beyond that, we now add in durability and the confidence of that for patients.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

And last on EYLEA for me is just kind of a bigger picture, how much of a role is there for the 2-milligram product over time? Is this -- would you expect this as virtually all converted over to HD over the next few years? Or will there...

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

Well, I think that for Regeneron, we want to participate in the market very appropriately. And we believe that physicians need to make the decision on what product to use. Having said that, we do position EYLEA HD in our promotion, in our clinical exploration from a medical standpoint as being the standard of care of the future, but it's up to physician choice. And if, for example, there's an indication that we don't yet have with EYLEA HD, EYLEA might be the best alternative.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Okay. Maybe pivoting over to DUPIXENT and the COPD opportunity. Just maybe help us a little bit in terms of do you anticipate there's going to be a lot of education required around this as it comes to market, or is this an indication that could ramp fairly quickly given obviously the data you presented and the unmet need in the space?

Marion E. McCourt - Regeneron Pharmaceuticals, Inc. - EVP of Commercial

So certainly, for our commercial team, nothing gets started, until we have an FDA approval. Having said that, as everybody here today knows, the unmet need in COPD is absolutely pronounced. And to have a product potentially approved in eosinophilic COPD and just in the G7 alone, we have about 500,000 patients with profound unmet need. We also have a company working with Regeneron in Sanofi, that are expert in the pulmonary space with DUPIXENT in asthma today.

So we do have the opportunity to be very impactful in the marketplace very, very quickly but won't get started obviously until we have an approval. But I will have to share that the unmet need and the enthusiasm for DUPIXENT in COPD is very, very strong. And for future product itepekimab, which George covered as well, different population of patients, that would be former smokers, but it's actually an even larger COPD population potentially.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

What Marion said -- sorry, George, go ahead.

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

I was going to say, or build on what Marion said, which is that we're already seeing pulmonologists for asthma. And in fact, there's a very common syndrome, which is known as ACOS or asthma-COPD overlap syndrome. And so, I think that there's a need for an agent here, and the physicians are already well aware of Dupi. And now you have a single molecule that can help both classes of patients that they deal with every day. So I think that that's going to be very important for how this is taken up.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Yes. I think I was going to make the same point. Physician experience is very important. Just like when all the dermatologists who are familiar with it for atopic dermatitis, the launch for prurigo nodularis went very well. We expect, as George was alluding to, the same thing, that the physicians who are prescribing for COPD are very familiar with the product because they're prescribing it for asthma.

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

And also, when there's a dire need, when there's nothing else, and this is a horrific, horrific disease that has such an impact on quality of life, let alone duration of life, people want something that has such meaningful impact; and even indications where we had no presence like EoE for gastroenterologists that have never heard of Dupi, tremendous uptake, because when you really have a game-changing medicine for a disease for which there is nothing and patients are crying out, I think that it's society's obligation to figure out how to get the drug to the patient.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Yes. I would say Sanofi and Regeneron are really working very hard to make this a very successful launch assuming that we get the approval in a timely manner, which we anticipate.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Great. The severe allergy opportunity, can you just update us in terms of what are the next steps to watch here as you push that forward?

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

Well, the next step is to actually do our clinical trial. When you think about the risk when you move agents into clinical trials for the first time is they've never been in humans. You've done some animal studies. How are they going to really work in humans? The beauty here is we know how these things individually work in humans. And if they just could do together what they do separately, you really have a potential cure for severe allergy. We did put them together in monkey models, and they worked exactly as they did in humans, and they seemingly cured severe allergy. So a lot of the risk is mitigated by having seen what they do alone.

We're now doing clinical trial, where, for the first time, we're putting them together with transient BCMA treatment followed by Dupi. If they continue to behave like they've behaved individually, this really can be, once again, a new game-changing approach for patients so much in need. And as we know, there are literally millions and millions of individuals suffering [from] severe food allergies and other severe allergies, impacts their life, food-restricted diet and so forth, other impacts, failure to thrive. So this could really be important for a lot of people.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

And the metrics are pretty good in terms of measuring sensitivity, skin sensitivity, or IgE levels, things like that. We should be able to get some real answers, as George suggested, in fairly small initial populations.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Great. Pivoting over to oncology. Can you just talk a little bit about the LAG-3 program? I know we're expecting data there. So maybe just a two-part question. First, confidence in terms of differentiation versus Opdualag? And then maybe second, beyond melanoma, how do you think about the biggest opportunities for this mechanism as we kind of broaden out?

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

Well, I think, as I said, in a way, we -- all of us who've been in the field have been a little disappointed in our ability to enhance the activity of checkpoint inhibition. The data that we've now actually seen in 3 separate cohorts that we've now treated in humans have really been very consistent, and the data is really much different than what's been seen before.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Can we put the slides up? It will help.

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

Yes. So if we reproduce what we've seen in our first 3 individual cohorts that we've tested in first-line melanoma and we get consistent data, this is really going to change the paradigm for these patients. And if we consistently see also the safety profile that we've seen, we haven't really seen enhanced immunotoxicities and so forth. So this is really an exciting program. And at the end of the year, we expect potentially pivotal data from our ongoing trial.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Last minute or 2 here. Just continuing on oncology. CD28 seems like really interesting approach. I know there was some toxicity dynamics you're working through. Maybe just, as you sit here today, level of confidence in this platform and approach relative to maybe where we were a year ago.

George D. Yancopoulos - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, Chief Scientific Officer & Co-Chairman

Yes. I think that, as you said, the efficacy that we saw -- I mean we're at the highest dose, these advanced prostate cancer patients who are on death's door, essentially within 3 weeks, completely eliminate all trace of cancer. I mean that's really unprecedented type of data. However, 2 to 3 patients had very severe immunotoxicities.

What we know from the science, from our preclinical models and so forth is, when you combine the CD28 pathway with cemiplimab as we did in those studies, you create polyclonal T cell activation and you can start now attacking the host, which is, I think, what we saw. When we do the same

CD28 but now when we combine it with our CD3 bispecifics, we don't see that in our animal models. So that's why, as I said, we're so excited now. The power of the CD28 is so unprecedented. It unleashes antitumor response to a level that [has] never been seen before against some of the hardest so-called immunologically cold tumors.

Now if we can just reproduce what we've been seeing in our animal models, combining it with the CD3 bispecifics can maybe get that same power, that same antitumor efficacy but without the severe immunotoxicities. And I should point out, a lot of people say, oh, animal models, mice models, they don't predict anything. Let me just remind you, Regeneron invented VelociGene technology, the world's greatest humanization technology. In our models, we humanize the whole system. So we're not really working with old-fashioned mice. We're working literally with almost little genetically humanized models.

And so far, almost everything that we've seen in almost every one of our disease scenarios in these humanized models is predicted, which is why, historically, we tend to have such high rates of success in our programs, because we have the human genetics data that predicts which targets we should go after, and we have the genetically humanized mouse models, which are literally like human beings, the little humans that we can do essentially our prehuman trials in.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Great. I think we stop time here. Really appreciate the comments today, and thanks for joining us.

Leonard S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Thank you, Chris.
