EDITED TRANSCRIPT

REGN – Regeneron Pharmaceuticals Inc. at J.P. Morgan Healthcare Conference

EVENT DATE / TIME: JANUARY 09, 2023 / 09:00 AM PST

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PRESENTATION

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

Good morning everybody. I'm Chris Schott, diversified biopharma analyst at JP Morgan, and it's my pleasure to be introducing Regeneron this morning. Representing the company, we have the company's co-founders CEO Len Schleifer, as well as CSO George Yancopoulos.

2022 is obviously a very successful year for Regeneron with the company making significant progress across its core drivers as well as its pipeline. We're very much looking forward to an update as how the team's thinking about 2023 and beyond. With that, I'll turn it over to Len.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Thank you. Go ahead, George. Come on up, Marion. Hello and good morning to everybody. It is really good to be here face to face. Dare I say, virus to virus, or variant to variant. I hope not. Anyway, we've got a lot we want to cover, so I'm going to jump right in.

I'm Len Schleifer, and this is our forward-looking statement. We'll be making a bunch of forward-looking statements. Check out our filings. There is risks associated with them. Read this, please, when you look over our material.

In 2022, we had three imperatives that we had to accomplish. First of all, we had to figure out what is our long-term strategy for EYLEA. When you look at the data with us and when we saw the data we've disclosed, it really eight milligram or high dose aflibercept really positions our retinal franchise for prolonged leadership.

We're very excited about the data. In fact, the data turned out better than, I think, our high expectations. The second thing we had to do is continue to demonstrate that Dupixent should be the leader and should continue to grow as the leader in type 2 inflammatory or allergic diseases.

There was talk about competition with oral JAKs and what have you, but Dupixent has really shown its colors in 2022. Let me just emphasize, for example, on the safety side.

The FDA has approved our drug for children, as infants really, as young as six months. That really speaks a lot to the safety of our product. It is the leading drug, and it's now approved in five different type 2 allergic diseases and with more to come.

We accomplished what we wanted to. That's the result of great collaboration and partnership with Sanofi, and that product continues just to drive forward, and I think it has a great future.

The third thing we needed to do was really convince ourselves, convince the scientific community, and then obviously

convince you that our oncology efforts were going to bear fruit. We've had a long-term strategy that George will get into in more detail.

We've always believed that Libtayo was foundational, our PD-1 inhibitor was foundational to that strategy. We acquired back half of the rights that we had licensed.

We now owned and control that product so we could put it together. We were able to put it together with really very promising data, both in the LAG-3 space and in our costimulatory space, which we'll talk a lot about in this presentation.

Finally, we have been trying to do our part to serve COVID. As you know, early on, we were able to really through a Herculean effort get a monoclonal antibody out there, a cocktail of monoclonal antibodies that could address a treatment paradigm for COVID.

We did this in record time, and it worked great for a while, but like many of these antibodies that have come forth, and now all of them, in fact, the virus has outsmarted them.

The virus has mutated in a way that the antibodies that you might make, and even in response to being infected with the virus, you might make in response to a vaccine, or you might get from us, all seem to be now being evaded by the latest strains that are taking over, such as the XBB.

The team has been hard at work, and I think we have hit sort of a jackpot antibody that George is going to tell you now about that we're going to push forward very rapidly.

Let me get into a little bit more detail on these topics. First of all, EYLEA. Look, EYLEA is just an amazing product. If you think about it, it is growing year-over-year at eight percent, and this is more than a decade into the product.

We anticipate, based on preliminary numbers for the end of the year, about $6.3 billion in sales in the US. We are the branded category leader with a 75 percent approximate branded market share.

The fourth quarter, everybody has been fussing a little bit about this, this morning, the sales of EYLEA were a little bit less than we expected. The sales were negatively impacted by a short-term shift to off-label Avastin. This was associated with the temporary closing early in the fourth quarter of a fund that provides patient co-pay assistance.

Our recent data has suggested that, now that this co-pay assistance is back and available, that the shift is reversing. We ended the late part of December, with the latest data we have, with a consistent 75 percent branded category share.

EYLEA is doing great. The long-term future of EYLEA, really, we think is in the data for eight milligram. I can tell you now that we did submit in December the BLA for eight milligram aflibercept.

We believe it has the potential to become the next-generation standard of care. We are starting to plan for pre-launch efforts anticipating, hopefully, approval sometime in the early second half of this year.

If you look at the data, and I must admit, we were really surprised. Even the KOLs, the pundits, everybody said, "Well, if you could get 35 percent of patients on the eight-milligram dose, 35 percent, if they could maintain intervals at greater than 12 weeks, you could have a really big product."

If you look at our data, we got 93 percent, more than 90 percent of people who were randomized to eight milligram were able to maintain dosing intervals of 12 weeks or more in our DME study.

That was also true in our AMD study. Once again, staggering results compared to the expectations, greater than 80 percent maintaining intervals of greater than 12 weeks. These data were really quite spectacular from our perspective. We

don't use that word too often, but they really exceeded, I think, everybody's expectations.

Just to put it in a little bit of perspective, and these are cross-trial comparisons. We don't have any head-to-head data. You should take this with some caveat. The data are what the data are, and you can't manufacture data unless you do studies.

If you look on the left side of this slide, the green represents patients in our DME study who were maintained on Q16-week dosing through the end of the 48-week experimental period. That's almost 90 percent.

On the right side of slide, you can see that that's a much smaller number were able to be maintained on that 16-week interval in the faricimab, or Vabysmo studies. These are staggering differences, different trial designs. You can hear arguments; well, is it really the drug or you did a different trial?

We could have, we should have, we might have, we didn't. Whatever it is, our data, I think, are really resonating well with the experts that we've shown.

It's also true in the AMD study, where once again nearly 80 percent maintained 16-week intervals with only a little bit more than 40 percent, 45 percent in the faricimab studies. We think these data say that the eight milligram aflibercept has the potential to become the standard of care.

Let me turn to Dupixent, which, as you know, we're in a collaboration with Sanofi. In the first nine months of the year, global product sales grew 41 percent, exceeded six billion dollars.

We had lots of regulatory progress. We had new approvals. We've got approvals in younger age groups, as I mentioned, as young as six months, approvals in eosinophilic esophagitis, prurigo nodularis.

We have an sBLA submitted for chronic spontaneous urticaria. These new approvals represent big new opportunity. If you attend Sanofi's talk, you'll hear a little bit more about what this means. This is a representation of our journey that we have taken with Dupixent, starting with atopic dermatitis, working our way through many opportunities.

Really, if you talk to some expert and you say, "How do you define a type 2 allergic disease," some experts will say, "Well, if it responds to Dupixent." It has become the standard, if you will, of type 2 allergic diseases.

There's an opportunity to expand even further into COPD both with our IL-33 antibody, as well as with Dupixent. Data coming up on Dupixent on the not too distant future fingers crossed there. Significant additional opportunity for the product.

Let me just close by saying in my part of my remarks is that oncology was something we've made a long-term investment in. We've got finally, Libtayo, our foundational drug approved for all people with non-small cell lung cancer in combination with platinum-based chemotherapy.

It's only one of two antibodies. Obviously, Keytruda being the other that's approved irrespective of the PD-1 expression levels or histology. We're excited about the possibilities for Libtayo, but what we're most excited about is what Libtayo can do in combination.

Let me turn it over to George, who's going to tell you a lot more about this and some of our other work. George, here's you.

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

Thank you Len. I want to start by reminding everyone of the keys to the Regeneron approach. When we founded the company, coincidentally it was exactly 35 years ago yesterday, we had the goal of using the power of science and

genetics to repeatedly bring new medicines to patients.

We soon realized that to do this, we had to revolutionize the technologies that could actually deliver new medicines, and in particular, create turnkey therapeutics delivery platforms. Our trap platform yielded Eylea and some more minor successes.

We then utilize our proprietary mouse genetics technologies to produce arguably the most valuable platform that produces fully human antibodies, notably our VelocImmune mouse, with a genetically humanized immune system that has delivered seven FDA-approved or authorized medicines, including Dupixent that you just heard about and Libtayo.

Many people realized how innovative we were in our early years, but what I am proudest of is that we have not lost our edge in innovation, but instead continually push that edge further and further forward. We have evolved our biologics platforms. We are now leaders not only in the human antibody arena, but with bispecifics and costimulatory bispecifics.

Over the last few years, we are becoming leaders in genetic medicines, starting with our Regeneron genetic center eight years. Leading to several successful collaborations in a series of novel, experimental turnkey therapeutic modalities from siRNA to CRISPR-based gene knockout and insertion, to viral-based gene therapy.

We're a very unique and rare company for our size whose innovation is still driving and filling its pipeline. On this slide we list significant pipeline advantages during '22, some of which were just highlighted by Len.

I'm going to focus on our advances in immuno-oncology where we think our pipeline can meaningly advance the standard care, multiple tumor types. This slide 18 delineates our immuno-oncology strategy, which is built on our turnkey therapeutics platforms that yield several different classes of therapeutics.

Including our immunomodulating checkpoint inhibitor antibodies, our CD3 bispecifics, and our co-stimulatory bispecifics, all of which were prospectively designed to be flexibly combinable in potentially synergistic manners.

All these classes were initially validated using our proprietary and highly predictive genetically humanized mouse models. Over the last few years, each class has been individually clinically validated in human trials.

Most recently, we have seen early clinical confirmation of the power of combinations of these classes, and I will focus on some of this recent combination data.

Slide 19 lays out our various stage clinical programs, which we have for each class as individual agents, as well as some combinations. I'll now focus on recent data for two of these specific exciting combinations.

Our PSMA by CD28, costim bispecific combined with cemiplimab in metastatic castrate, skin resistant prostate cancer, and fianlimab, our leg three antibody in combination with cemiplimab in metastatic melanoma.

Starting with our PSMA by CD28 combination. Last August, we announced the first clinical data in metastatic castrate resistant prostate cancer patients. A tumor considered immunologically cold and largely unresponsive to PD-1 monotherapy.

We helped combining costim bispecifics with PD-1 could confer responsiveness to such cold tumors. At the five lowest combination doses, there was almost no evidence of clinical activity as you see on the upper right.

At dose level six to eight, as seen in the bottom right, we began to see clear evidence of dose-dependent antitumor activity. Importantly, grade three or higher immune-related adverse events only occurred in patients with antitumor responses.

On slide 22, we provide some incremental updates on this data. On the left, you can see graphs depicting PSA responses in three of the four patients at our highest dose. In these patients, the PSA tumor biomarker continued to rise during the three week PSMA by CD 28 monotherapy leading.

Soon after concomitant administration of Libtayo, you can see dramatic PSA reductions exactly as we predicted from our preclinical studies. In terms of longer term follow up, we can report on our first responding patient, or our index patient, who also experienced a dramatic reduction in PSA shortly after Libtayo co-administration at week three, as you see for these three patients.

This index patient discontinued treatment after seven weeks due to an immune-related adverse event. The AE has resolved and he has not received any subsequent prostate cancer treatment, yet his complete response has endured for over a year and a half.

His PSA remains below detective levels, his soft tissue lesions disappeared, and his most recent bone scans normalizing with a negative PSMA PET scan. A truly remarkable success for a patient previously thought to be terminal and non-responsive to PD1 immunotherapy.

These very encouraging initial data for our PSMA by CD28 co-stimulatory bispecific provide the first clinical evidence, supporting the promise of this exciting and entirely new class of immunotherapies. This slide provides our already extensive list of clinical or near clinical costim bispecifics and their various ongoing or upcoming combination trials.

We not only have the ability to combine these with Libtayo as I just showed for PSMA by CD28, but with our CD3 bispecifics. Such combos have profound activity pre-clinically. As I already mentioned, we have validated our CD3 bispecifics as individual agents in the clinic.

Many with first in class or best in class activity, but we now have the ability to take these to the next level by combining them in a logical manner with our costim bispecifics. Along these lines, we anticipate dosing our first DLBCL lymphoma patient with our CD22 by CD28 costim in combination with our CD20 by CD3 bispecific in the first quarter.

We also expect to update on several of these programs this year. On slide 24, we talk about now an another exciting recent advance with combination immunotherapies involving fianlimab or LAG-3 antibody in combination with Libtayo.

Last year we reported that this combination showed consistent and strong efficacy in two independent cohorts in melanoma, and also promising early activity in an expansion cohort in non-small cell lung cancer.

These data supported our initiating a robust clinical development program in melanoma, and we also plan to initiate Phase two-third studies this year in non-small cell lung cancer.

This slide 25 summarizes the combination data I just referred to, which we recently reported at ESMO, showing a second cohort in first-line metastatic melanoma that confirm the promising data we had seen with an earlier cohort.

Both cohorts demonstrated overall response rates of over 60 percent for the fianlimab/cemiplimab combination with pooled median progression-free survival of 24 months. These data compare very favorably to the FDA-approved and now new standard nivolumab/relatlimab combination, which had an ORR of 43 percent and a median PFS of 10 months.

Importantly, the fianlimab/cemiplimab combination had a safety profile that was comparable to anti-PD-1 monotherapy. This slide 26 lists our upcoming oncology data readouts. As you can see, we have a busy couple years ahead.

In addition to our 2023 data disclosures, we also anticipate BLA submissions for odronextamab in two kinds of lymphoma as well as for linvoseltamab in myeloma.

Moving now beyond immuno-oncology, and as Len mentioned, we continue to use our antibody technologies to play our part in the COVID pandemic. Despite mass vaccinations, millions of immuno-compromised people in the United States alone don't adequately respond and are less vulnerable.

Monoclonal antibodies could help protect and treat vulnerable patient populations like these, but viral variants rendered obsolete all previously authorized antibodies, including our REGEN-COV, which had helped so many.

We have one of the most sophisticated and largest screening efforts for COVID antibodies, and we believe we have identified one-in-a-million antibody that works very differently to all prior antibodies by binding outside of the immuno-dominant highly variable RBD and NTD domains.

These domains have been the primary site of antibody binding and correspondingly of variant mutations. We have caused the initial vaccines in previous COVID antibody therapies to lose their activities.

We hope that by binding outside of these domains to a unique targeted epitope that is highly conserved, with over 99.9 percent conservations since the beginning of the pandemic, it will lower the risk of losing activity against future variants.

Importantly, this antibody, known as REGEN14287 demonstrates high neutralization potency against all known SARS-CoV-2 variants and lineages to date. Activities enabling clinical manufacturing have commenced, and we expect to enter clinical development later this year.

Finally, I want to go back to the beginning of my section where I talked about how everything starts with our innovative turnkey therapeutics platforms and how these platforms are helping make us leaders in biologicals and in genetic medicines.

Now, I want to highlight how these are coming together in a novel way, using biologics to allow specific tissue targeting of genetic medicines.

Major limitations of genetic medicines is delivery of the genetic payload to the cells of interest in the body. Currently, systemic delivery is largely limited to the liver and local injection is limited to a couple of sites.

Regeneron has invented a proprietary approach that builds on decades of our antibody experience, so as to use antibodies to deliver genetic payloads to specifically targeted cells in the body, and we have validated this approach in non-human primate studies.

With this antibody targeting technology for systemic genetic medicine delivery, we believe we can empower the winners in the gene medicine field and become a leader ourselves in gene medicines by combining these unique targeting approaches with innovative payloads across many disease settings.

This slide depicts our current clinical stage pipeline of our approved products, as well as over 30 product candidates, all of which were developed with the technology platforms I discussed earlier, as I said, a rare example where our own innovation is driving our pipeline.

This indicates upcoming submissions, and we have a new wave of submissions coming over the next few years. These list our anticipated 2023 milestones, which span ophthalmology, immunology, oncology, and immunology.

I wanted to close with something core to how we operate our company. Since our founding, Regeneron's mantra has always been doing well by doing good. With the mission of using science to improve lives, we recognize that acting responsibly is crucial to ensuring that we can continue to deliver new medicines to patients and needs.

Along these lines, I'd like to highlight our STEM efforts to engage and inspire the next generation of scientist-

entrepreneurs. Towards this end, we have committed over $100 million to support the premier high school science competitions, that is the Regeneron Science Talent Search and the Regeneron International Science and Engineering Fair.

These are the very competitions that got both me and Len and many of our generation, our starts in science, when they were sponsored back by Westinghouse and then Intel. We are sure that they will deliver scientific leaders of the future.

With that, I thank you for your attention. Now, I would like to thank everyone and hand it back to Chris for the Q&A portion of our presentation. Marion, our head of commercial, will join Len and myself for the question-and-answer period.

QUESTIONS AND ANSWERS

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

Great. Thanks. Thanks very much for those comments. Maybe just to kick off the Q&A, talk a bit more about EYLEA. I know you had the fourth quarter results out today.

You referenced some of the short-term uptake of Avastin. Just elaborate a little bit more on what the dynamics are. I think you referenced in the comments that you're seeing some of this normalize as you're getting later in the quarter. Just maybe share a bit more there?

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Yes. I mean, the sum and substance of it all is that the EYLEA marketplace is sensitive to co-pay assistance. When that co-pay assistance is not available, patients are forced to go to what has been proven to be an inferior product, unfortunately, which is Avastin compounded.

Very early in the quarter, there was a disruption in the co-pay assistance, and that quickly moved patients from branded EYLEA to Avastin. That has been resolved. They are fully back in full funding.

I think of this as a sort of short-term blip, which should not affect the trajectory of the molecule at all. In fact, in late December, our branded market share remained at a consistent 75 percent. Frankly, I think this is really much ado about an unfortunate transient episode.

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

Yes, absolutely. I know you shared some of the data in the presentation. Regarding Vabysmo, share a bit more what you're seeing in the market. Especially when you think about the eight mg coming, you've got a very differentiated profile. What are you seeing in the near term before that?

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Marion is closest to that. Maybe, she can comment.

Marion McCourt - *Regeneron Pharmaceuticals, Inc., Executive Vice President-Commercial*

Sure. I'm very happy to, and good morning to everybody. I would say that the very competitive profile we see with EYLEA

is the most important element.

As Len described today, the results of the year, the eight percent increase in overall net sales. Now, to characterize the competitive dynamic, the breadth of indications, our visual acuity, safety, efficacy are really what physicians are looking for.

Probably best to ask my competition about competitive product uptake. I want to answer your question. We would say it's probably been low-modest at this point, and I think the issue of the sustainability, durability of efficacy is something that perhaps over time will be seen.

Where the greatest enthusiasm is really is for our aflibercept eight mg product. We'll look forward to additional clinical discussions, the FDA review, and share with all of you that our team is really excited about potentially launching that product later in the year.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Yes. Consistent with what Marion said, and we're keeping a close eye on this, we're seeing switches back from Vabysmo to EYLEA. That's an interesting indicator.

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

Longer term, in terms of the growth of the overall market, anything changed in your view in terms of the sustainability of growth for the category?

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

No. I think what's driving the category are demographics, aging of the population, as well as increase in diabetes and diabetic eye disease.

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

You probably are not going to share your full commercial strategy at this point, but just help us contextualize, once eight mg approved, how we can think about the velocity of conversion away from the two mg. So, thinking about later this year into '24?

Marion McCourt - *Regeneron Pharmaceuticals, Inc., Executive Vice President-Commercial*

I would say, we have an amazing opportunity in a market that we know very well with our Eylea today. When you start looking at the clinical data for Aflibercept 8 mg, it gives the possibility of patients having the same sort of clinical effect improvement in their vision and safety, but not having as many injections.

For anyone thinking about saving their vision, of course, you would have an injection in your eye, but for everyone who's involved with treatment, the providers who take care of them, and the volume of patients coming into offices, this ability to extend durability of product.

As we're looking at the data today, getting patients out to 12 weeks or more, is really very important. When we think about strategy and possible product uptake, we're looking at a situation where physicians could look at making a choice for

initiation of therapy. They could look at choice for patients already on therapy.

How we actually bring strategies into the market remains to be seen, but most important to us is that physicians are able to make the choice that's right for their individual patients and their patient characteristics.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

It's a bit funny, we constantly talked about fewer injections, fewer injections, but what we shouldn't forget is that they've been a ton of injections, nearly 60 million injections since the launch of Eylea. That's a remarkable testament to the product safety and efficacy.

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

Just to sum up on this, it seems like you had a blip in the quarter, thinking out to next year, that normalizes and just all speed ahead, watching for the 8 mg. Is that a fair way to think about it?

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

That's a fair way to think about it.

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

Pivoting over then to Dupixent, you've got a growing set of indications. Talk a bit about what you see as the biggest opportunities for growth in that asset as we think about the suite of areas you can go with this.

Marion McCourt - *Regeneron Pharmaceuticals, Inc., Executive Vice President-Commercial*

I'm happy to start. I would say when we think about Dupixent first, think about the existing indications, think about atopic dermatitis, where even today, we haven't even begun to get into the full potential patients who could benefit from this transformational therapy.

Think of adults, think of adolescence, and think of our youngest patients, and the more recent indication we launched for little ones, six months and above, which frankly is really important to the treatment atopic dermatitis, because for all patients, it's an element of reassuring everyone of the safety coupled with the efficacy of the product.

Obviously, beyond atopic dermatitis, patients sometimes are troubled by more than one type II allergic disease. That same atopic dermatitis patient might have asthma, they may have other type II conditions. It's a really important element of the Dupixent profile.

Then to your question of future growth, it is a land of riches for the commercial person and my commercial team, because even in this past year recently, we launched Eosinohilic Esophagitis that added in a very important population, just in the US, about 50,000 patients. We also launched for Prurigo Nodularis, that was a population in the US of another 75,000 patients.

The data goes on with indications coming this year. We're obviously excited about all the indications, but COPD is probably one that could have a remarkable impact on patient opportunity and making a difference with patients struggling with COPD, that population is about 500,000 in the US.

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

When I think about the competitive dynamics, Rinvoq launched, obviously had very strong performance for Dupi in '22. As I think about lebrikizumab coming to market, how do you think about that as a potential competitor?

Is that essentially something that could be more impactful to Dupixent, or do you think with the breadth of indications, etc., that's not concerning?

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

There are two things to comment on that. First of all, there's plenty of room for more than one drug. You're looking at psoriasis world, how many different drugs who are in the inflammatory bowel disease, rheumatoid arthritis, we barely scratched the surface.

In terms of the advantage we have, it's what George has been emphasizing all along as we developed this molecule, is that you have more than one disease that lebrikizumab is not going to be able to address when they launched this product, who knows, even down the road.

I think that product may not have been able to work when it was tested in asthma in a prior existence. The fact that we have Dupixent, which can address more than one type II disease, mind you, it's not like the type I diseases where if you have psoriasis, you tend not to have rheumatoid arthritis, kind of thing.

Here, you actually tend to have...George, what's the number? How many people have asthma in our stat files? I don't know.

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

For example, in most of our trials when you look at one disease like atopic dermatitis, more than 50 percent of the patients have another comorbid allergic disease, many of which are also treated with Dupixent.

This just shows the power, allergy is a systemic disease, sometimes it manifests mostly in the skin, but it also is occurring simultaneously in the lungs and the upper respiratory system. Dupixent allows you to treat all of these.

As Len said, when you use other drugs like lebrikizumab, basically it's only addressing part of the pathways, and only treats some of these diseases. It's not treating the systemic disease that's occurring throughout the patient's body.

I think that any treating physician, if they're trying to do the right thing by the patients, would give them the drug that treats systemically the cause of the disease.

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

The breadth of label really differentiates and protects the franchise. Pivoting a bit over to oncology. Obviously, some pretty exciting data on the costim side. When I look at or think about the PSMAxCD28, the data you've seen so far, maybe just help us put some of this into context.

At the heart of it how derisked do you see this approach at this point based on what you've seen so far?

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

I think it's not over-stating it that this may be one of the biggest breakthroughs in the history of immunotherapy. Think of what we've done, the field has been talking about cold tumors that don't respond to immunotherapies, particularly PD-1 therapies. That's the vast majority of cancers.

We came up with an approach entirely in-house, which came up with a targeted way that we can now activate immunotherapy in cold tumors in combination with either PD-1, or with CD3 bispecifics on a tissue cancer specific manner.

Of course, we had incredible animal data using these very proprietary and very well validated and unique, genetically humanized mouse models that we use. Until you prove it in humans, you don't know. The data was really stunning. Len said, Eylea performed unbelievably in its setting, Dupixent continues in its setting.

Now we have this entirely new class of cost in bispecifics that have seemingly just taken immunotherapy to the next level. As I just showed you, in the highest dose level, three out of the four patients had these incredible rapid responses in otherwise terminal patients.

Our index patient is now out more than a year-and-a-half, looking like a complete remission. These are really staggering data. As we showed you, we already have in the clinic a pipeline of these with a whole myriad of combination opportunities.

We really think that this has a real chance to change the face of cancer treatment and allow so many of these patients who desperately need something to have a real opportunity to fight back against their cancers, using their own immune systems. Very exciting.

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

As we think about the PSMA data and the work you're doing, what can be done to address safety here? I know on a positive side, really seems to be correlated with efficacy, but talk about the efforts to maybe balance out that, that overall profile.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

I think that activating the immune system, we know with the PD-1 therapies comes with a cost. That at times you will get some autoimmune reactions that can cause problems for the patients. We see this, since we are giving a more powerful anti-cancer therapy, there will be some more concern about some of these autoimmune responses.

In patients who otherwise have no other options, their lives are literally at stake, looking at the results that we've already seen, the benefit/risk ratio seems to be in favor of treating patients who are otherwise, unfortunately, without any other options and at death's door.

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

As, Chris, you mentioned, just what's repeating what you said, and I think it was in George's presentation as well, that the side effects were seen in the patients who were benefiting, that really changes a risk/benefit analysis.

If you're treating 100 people and you're helping 50, but you're harming 100, it's a lot different than if the people who are really benefiting are having some of these immune reactions, which is what we've seen.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Very important point.

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

Just a couple of quick ones on this. Once you land on the right dose later this year, is there a pathway that you can accelerate a filing here? As you mentioned, these are patients that have very few options. You're getting very profound responses.

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

Yeah. As we've already done in other settings, we think that we can get an accelerated filing in these late-stage patients who have run out of other options, where we can demonstrate this profound activity with a suitable benefit/risk ratio.

As Len said, very critically important. I'm glad he made the point. Only the patients with benefits seem to be having these immune-related adverse events.

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

Then, the last one on this, when I think about moving into other CD28 kind of opportunities, will there be an ability to progress the Phase 1 studies faster now that you may have a better understanding of this, or are these always going to be fairly slow going, just to the nature of the...

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

We hope. It's always a negotiation with the FDA. They're always concerned. Certainly the reason they were so concerned here, there was some real disasters with people trying to take advantage of CD28 before. In order to avoid those, we came up with this very targeted approach.

We seem to have avoided the problems that the earlier non-specific approaches had. We hope the FDA will correspondingly recognize this, and allow us to move faster with these class of agents as we have them going forward.

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

This is my last question for me. You mentioned COVID antibody that seems to have a pretty unique profile. Just make us a sense of how quickly that could move forward and how much capacity the organization could build with that.

George Damis Yancopoulos - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Scientific Officer & Director*

We've shown before that we can move very quickly and we have capacity to treat millions of patients. It's going to be less limited by our technologies and our capability than our discussions and negotiations with the FDA.

Also at the time that we're doing our clinical studies, what kind of studies will be required by the FDA part of that

negotiation. Also, the prevailing amount of disease, which obviously would allow any studies to go more quickly.

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

I think we're just about time. Really appreciate the comments day and thanks for joining us.

Leonard S. Schleifer - *Regeneron Pharmaceuticals, Inc., Founder, President, Chief Executive Officer & Director*

Thank you for having us.