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OVERVIEW:

Company Summary

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PRESENTATION

Christopher Schott - JPMorgan Chase & Co - Analyst

Good afternoon, everybody. I'm Chris Schott at JPMorgan, and it's my pleasure to be introducing Regeneron today.

From the company, we have Regeneron's Co-Founders and Co-Chairs, President, and CEO, Len Schleifer; and President and CSO, George Yancopoulos. Between the core portfolio and an increasingly broad pipeline, I'm very much looking forward to the presentation today.

So with that, over to Len, and we'll go to some Q&A after that.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Thanks, Chris. It's great to be here. We're going to try and do maybe 20 minutes of presentation and then leave it to you for questions.

It's great to be back in San Francisco for the 44th, I guess, JPMorgan Conference. We think it's a very interesting conference. It mainly got interesting 37 years ago when we started presenting. We have been in every room at the conference. And in every single room many times, the most common phrase that we have heard, so it shows how consistent the place is, is promising data.

Okay. We -- that went over well. As my team said, don't do it, Len. Anyway, I'm Len Schleifer, CEO of Regeneron. I'm joined on stage by my longtime partner at Regeneron, Dr. George Yancopoulos, Regeneron's Chief Scientific Officer and Co-Founder. During our presentation, we will be referring to slides, which may be found on our website.

This is one of my -- this one is one of my favorite slides. It contains our forward-looking statements. There's 44 lines in there. We've added one line each year. And you should read them carefully and understand there are a lot of risks of what we say and refer to our SEC filings for more detail. With that underway, let's get started.

Let me start by providing a brief overview of Regeneron, a company that has proven itself to be truly unique, I think, in the biopharmaceutical industry. Our strategy is deeply rooted in following the science. It's a phrase that many people use, but it's one that we truly live by. And we harness the power of science and Big Data to consistently deliver transformative therapies to patients.

Over the past 10 years, George and the team have created a powerful tool kit of proprietary turnkey technology platforms such as VelocImmune, Veloci-Bi, and the Regeneron Genetic Center that provide Regeneron's secret sauce. These platforms enable rapid and efficient drug discovery and development, enabling us to screen thousands, if not millions of antibodies, significantly increasing our likelihood of identifying the optimal candidate.

Regeneron is also recognized as a pioneer in bispecifics, genetic medicines as well as a leader in genomics and proteomics-based Big Data in the healthcare space. While we did not invent genomic sequencing or proteomics, we have pioneered the high throughput aspect of that, creating affordable technologies which allow us to apply these game-changing approaches to millions and millions of people.

And while AI approaches can be powerful, they are very limited by the amount of genomics and proteomics data available for healthcare discovery and management. We believe in this area, we stand alone on our Big Data assets. Driven by this science-first and Big Data approach, our pipeline now includes 45 clinical candidates across six major therapeutic areas. This breadth reflects our dedication to tackling a wide spectrum of unmet medical needs and establishes a strong foundation for continued success.

With 14 internally discovered therapies that have been approved over the past 15 years or so, Regeneron has averaged roughly one new approval per year and has demonstrated the ability to repeatedly deliver important therapeutic breakthroughs.

Regeneron's commitment to innovation has resulted in a portfolio of brands that continue to deliver sustainable growth. In the fourth quarter of 2025, our retina franchise reported combined US net sales of $1.1 billion for EYLEA HD and EYLEA. Fourth-quarter 2025 EYLEA HD net sales in the US were $506 million, up 66% versus the fourth quarter of 2024 and up 18% sequentially versus third quarter of 2025 driven by a 10% increase in physician demand.

EYLEA HD's label was expanded in late November to include every four-week dosing and the addition of macular edema following retinal vein occlusion, further enhancing its commercial potential.

The mix of our franchise net sales has been steadily shifting towards EYLEA HD since launch with EYLEA HD now comprising nearly half of net sales.

Importantly, we submitted an application for a new filler for the EYLEA HD prefilled syringe, with an FDA decision anticipated in the second quarter of 2026 this year, and the FDA also recently approved an alternate vial filler for EYLEA HD.

Turning to Dupixent, a drug we commercialize with Sanofi. Dupixent has become the world's most widely used branded antibody with over 1.3 million patients actively treated worldwide.

As we first predicted here at the JPMorgan conference about a decade ago, Dupixent is delivering on its pipeline in a product promise. Dupixent is now approved for eight different diseases driven by type 2 inflammation and leads in new-to-brand prescription share and total prescription share in seven of these indications. With annualized global net sales exceeding $19 billion based on third-quarter net sales, which grew 27% year over year, Dupixent is positioned for sustained growth.

And our most recent blockbuster, Libtayo continues its strong growth as the leading immunotherapy for advanced non-melanoma skin cancers. Libtayo is now the only approved IO treatment for adjuvant CSCC, an indication with 10,000 addressable patients in the US alone, which we believe could be a blockbuster commercial opportunity in and of itself.

Libtayo also continues to make significant inroads in lung cancer and is now the second most prescribed I-O treatment in first-line advanced lung cancer in the US.

Our capital allocation strategy prioritizes robust investment in internal research capabilities, which we believe offer the highest potential return for our shareholders. We expect to invest approximately $6 billion in R&D this year, as well as over $7 billion of capital investments in the US in the coming years to support our R&D and manufacturing capabilities.

Regarding external innovation, we are constantly evaluating opportunities with a particular focus on platforms and technologies that enhance our core strengths or accelerate our existing development strategies.

Our business development efforts have delivered meaningful results. For example, our collaboration with Alnylam, including the in-licensing of cemdisiran which has enabled us to independently pursue development in generalized myasthenia gravis as well as other complement-mediated diseases.

More recently, we in-licensed olatorepatide, a GLP/GIP receptor agonist from Hansoh to accelerate our strategy in obesity and entered into multiple gene editing collaborations with Intellia, Mammoth, and Tessera. After investing in R&D and business development opportunities, we return excess cash to shareholders. We view opportunistic share buybacks as an efficient use of capital and initiated a modest dividend in 2025. Altogether, we returned $3.8 billion to shareholders in 2025 alone through buybacks and dividends.

I'd like to say a few words on why our mix of R&D spend is more focused on internal investment than our peers. While other companies on average dedicated almost half of their R&D investment to external business development, we have historically concentrated about 95% of our resources on internal initiatives.

We do this for two reasons. First, we have the benefit of an extraordinarily productive R&D organization. Second, our internal analysis shows that the overall return on external business development throughout the industry has been modest, with only a small percentage of deals leading to successful approvals and even fewer still to commercial success.

Large M&A deals, in particular, have often resulted in value destruction. These data underscore the importance of investing in our sustainable innovation engine. By focusing on internal R&D, we avoid the inevitable pitfalls of becoming overly reliant on external deals to replenish pipelines and in most cases, dramatically overpaying. Instead, we have built and continue to invest in a robust, sustainable pipeline that we believe can deliver long-term shareholder value.

Let me briefly move on to our pipeline. We are investing in large categories across multiple therapeutic areas that collectively address a global market opportunity of over $200 billion.

With that, I'd like to turn it over to George for a deeper dive into our pipeline, and that will be followed by questions and answers. George?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Thanks, Len. I'll dive right in and to expand on Len's last slide. This showcases several of our key clinical programs from our broad pipeline, expected to generate clinical data over the next few years. with each representing a significant opportunity to advance care and address medical need in various unmet need areas.

Our pipeline features antibodies, bispecifics, siRNAs, AAV gene therapies, CAR-T, other cell therapies, peptides, and gene-editing approaches as well as novel combination across these modalities. While time doesn't permit a deep dive into every program, I'll use the next few slides to spotlight those with exciting near-term impact.

And let me start by highlighting several initiatives with our immunology and inflammation franchise aimed at maintaining our leadership in this field. Our multifaceted strategy includes exploring longer dosing intervals for Dupixent and developing innovative, VelocImmune-derived, fully human, long-acting IL-4R alpha, IL-13, and IL-4 antibodies with enhanced binding properties for these drivers of type 2 inflammatory conditions.

Notably, we are pursuing an expedited clinical development plan for our interleukin 13 antibody, which will enter the clinic shortly, ensuring we remain competitive in terms of timing with other industry players that are pursuing similar approaches.

Going beyond the Dupixent related opportunities and following similar strategies that we pursued with Dupixent, our Regeneron Genetics Center has identified multiple additional genetically defined I&I targets, each with the potential to become our next pipeline in a product. We will soon be bringing the first of these candidates into clinical development.

We are also advancing opportunities to treat or cure allergies following two distinct approaches. One that is allergen-specific where we have Phase 3 programs underway to treat cat and birch allergies and another approach that seeks to eliminate all immunoglobin E or IgE-driven allergies.

We have previously discussed our novel approach of reversing severe food allergies by transiently treating with Lynozyfic, our BCMA by CD3 bispecific, so as to rapidly eliminate the allergy-causing IgE-producing plasma cells, followed by long-term Dupixent treatment to prevent their return. We have now achieved proof of principle with this approach, with all four of our first patients treated achieving greater than 90% sustained reductions in their IgE levels.

We also plan to advance to the clinic novel therapeutic candidates designed to more specifically eliminate the IgE-producing cells as a follow-up approach that may prove more rapid and with broader allergy applications. Together, these efforts position us to maintain our I&I leadership and unlock new growth opportunities.

Let's now shift our focus to five key late-stage programs that are poised to deliver meaningful advances over the next few years across multiple therapeutic areas, including solid tumor oncology, myeloma, complement-mediated diseases, anticoagulation, and obesity. These registrational studies are already ongoing or will commence shortly. We expect a steady stream of critical data readouts from these studies starting the first half of this year.

Let's start with our checkpoint inhibitor program involving our LAG-3 antibody, fianlimab in combination with Libtayo, where our proof-of-concept clinical data showed that this combo may be very much differentiated when compared to the standard of care in first-line metastatic melanoma. We're excited for the upcoming readout of our pivotal trial, which is investigating this combination versus pembrolizumab monotherapy with data anticipated in the first half of this year.

Moving to Lynozyfic, our BCMA by CD3 antibody, which was approved in the United States last year in late-line multiple myeloma based on best-in-class data as a monotherapy in this late-line setting, with nearly double, let me repeat that, nearly double the complete response rates of other BCMA by CD3 bispecifics with similar follow-up.

Because of this rather remarkable monotherapy activity, we are undertaking an ambitious development program to drastically simplify the existing treatment paradigms, exploring monotherapy as well as combinations in early-line settings, which currently are dominated by highly complex, intense, and burdensome triple and quad drug combinations.

As we detailed at our Regeneron Roundtable last month, we have already generated compelling initial data with these monotherapy approaches in earlier line settings in lead-in portions of our pivotal Phase 3 trials. In fact, in all evaluable patients in the first-line setting treated with monotherapy at the planned Phase 3 dose, 100% achieved MRD negativity.

Beyond malignant myeloma, we have a differentiated strategy in precursive conditions to myeloma, where we are generating exciting early data that support our ambition to treat patients early and potentially prevent progression to the malignant disease through early intervention. Once again, in the precursor smoldering setting, 100% of evaluable patients treated with Lynozyfic monotherapy achieved MRD negativity. With four registrational studies now underway and four more initiating this year, we continue to advance our differentiated approach of pursuing monotherapy or simplified combinations across many and early settings.

Another exciting program in our pipeline is for complement inhibition. This program includes both an siRNA and an antibody, both targeting the complement component C5. The siRNA, cemdisiran, lower C5 target burden; while the antibody, pozelimab, blocks circulating C5, enabling together near complete inhibition.

We're using a customized and tailored approach to treat different diseases that require different levels of target inhibition so as to maximize efficacy. For example, in paroxysmal nocturnal hemoglobinuria, or PNH, where the current standard of care do not achieve optimal inhibition, we have shared results from the lead-in portion of our pivotal Phase 3 trial, which compared our siRNA antibody combination against the current standard, the antibody ravulizumab.

Remarkably, only 4% of patients treated with our C5 combination did not achieve LDH control. In contrast and consistent with historical data, about one-third of patients treated with the standard of care did not achieve LDH control. Even more impressively, after switching those uncontrolled subjects on standard of care to our siRNA combination -- antibody combination, almost all were able to rapidly and durably

achieve LDH control, giving us a lot of confidence that this combination could become the new standard care for PNH, with pivotal data expected late this year or early next.

In generalized myasthenia gravis, we reported last year that cemdisiran monotherapy alone delivered positive Phase 3 results, showing potentially once again best-in-class efficacy and safety with a highly differentiated every three-month subcutaneous dosing regimen.

In the pivotal NIMBLE study, cemdisiran achieved a 2.3 point placebo-adjusted improvement in the MG-ADL score at week 24, the best result among C5 inhibitors to date. We are on track to submit our US regulatory application to the FDA in the first quarter of 2026, with potential approval anticipated later this year or by early next year.

Finally, we anticipate completing enrollment for the lead-in cohort of our initial Phase 3 geographic atrophy study, exploring these C5 blocking agents in the first quarter of this year with preliminary results expected in the second half of the year.

Building on our hematology efforts. Factor XI antibodies represent the next wave of innovation and into coagulation, with the potential to expand into large underpenetrated markets. We all have to understand that clot prevention remains a critical unmet need. And one reason is that less than half of eligible patients receive therapy, primarily due to bleeding risk concerns.

Our goal with our Factor XI antibodies is to develop safer anticoagulants, reducing the bleeding risk while maintaining efficacy and allowing much broader utilization. Our two mechanistically distinct antibodies enable a tailored approach. One antibody is designed to optimize anticoagulation activity, while the other is designed to further minimize bleeding risk.

And our initial clinical data support our customized approach with impressive efficacy while suggesting a favorable bleeding profile when compared to current standards of care. Our data support development in multiple indications from postsurgical VTE prevention to stroke prevention in atrial fibrillation with multiple additional Phase 3 trials set to initiate in 2026.

Lastly, just as we're redefining anticoagulation, we're also pursuing transformative opportunities in obesity, a therapeutic area with enormous unmet need and significant commercial potential. While we are excited about our monotherapy capabilities with our in-licensed GLP agonist olatorepatide, or OLA, we are fast-tracking programs combining OLA with our proprietary antibodies addressing obesity-related comorbid conditions.

For example, about half of obese patients also suffer from hyperlipidemia and the associated cardiovascular risk, and GLP agonists do not adequately address this as they only lower LDL cholesterol by less than 10%. Therefore, we plan to more thoroughly address this unmet need by combining OLA with Praluent, our PCSK9 antibody, which has demonstrated more than 50% LDL lowering with cardiovascular disease prevention as demonstrated in large cardiovascular outcome studies.

Our plan is to provide patients with a co-formulation of OLA and Praluent that can be administered with a similarly convenient and affordable once-weekly injection as the current GLPs, but now adding on the important benefit for the large unmet need for those obese patients with hyperlipidemia. Regeneron is uniquely positioned for this opportunity with clinical studies expected to begin later this year.

Before I hand it over to Chris for some Q&A, I'd like to point out that we've only had time to touch on a small part of our pipeline. I'd like to highlight two more programs that have the potential to benefit children suffering from serious health challenges. And while these programs may not have enormous commercial potential, they help remind us what our business is really all about.

First, our innovative gene therapy approach, DB-OTO, which miraculously restored hearing to children born genetically deaf and which the FDA has recognized with its Commissioner National Voucher Program, allowing potentially accelerated approval this year.

Second, our therapeutic antibody, garetosmab, which has demonstrated an ability to stop in its tracks, a progressive and debilitating disease in which the soft tissues of the body are replaced by bone, so-called Stone Man Disease, leaving people unable to move their muscles and even to breathe. And this approach can also be potentially approved later this year.

So as I said, while these may not have huge commercial impact, for us at Regeneron, it really inspires us to keep doing what we're doing, which is trying to bring innovative new approaches to the biggest opportunities, but also to those with the greatest need.

So with that, I'd like to thank everyone for their attention and hand it over to Chris for some Q&A.

QUESTIONS AND ANSWERS

Christopher Schott - JPMorgan Chase & Co - Analyst

Great. I appreciate all the comments there. Maybe start with the discussion, I want to touch on I&I and appreciate some of the updates we had there. Maybe first, can you just clarify these incremental opportunities you're talking about? Are these generally going to be part of the Sanofi collaboration? Or it seems like some of these are going to be developed by Regeneron on a standalone basis? Can you just talk through the -- how you thought about going forward with these.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Sure, Chris. So obviously, the total unique programs have nothing to do with Sanofi. Some of the things that George referred to as exciting new targets that have nothing to do. But closely related to Dupixent, some, one in and others not. The long-acting Dupixent because it targets the IL-4R alpha, that's covered by the collaboration. The IL-13, the IL-4, the bispecific for IL-13, IL-4, those are not part of the collaboration. That doesn't mean they can't be part of the collaboration in the future, but right now, they're not.

Christopher Schott - JPMorgan Chase & Co - Analyst

And can you just elaborate a little bit more on those novel agents, what you're hoping to achieve in terms of profile relative to a fairly high bar that you have with Dupi?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Yeah. You hit the nail on the head. It is very, very difficult to improve upon Dupixent. It is the most broadly used antibody in the world, 1.3 million people take it. It has a remarkable track record of safety and efficacy driven by the genomics that George referred to, developed in collaboration with Sanofi. So it is hard to beat that.

When you have such great efficacy, eight for eight in clinical trials more coming and a wonderful really remarkable safety profile. But nevertheless, there may be some settings where you would like to have be able to give a longer acting Dupi as an example, maybe instead having to give it every couple of weeks, you could get every couple of months or every quarter or longer, and that you may be able to get there with some of our long-acting agents.

It is hard to imagine that one can actually improve upon the safety and efficacy, but we could improve upon some of the convenience factors.

Christopher Schott - JPMorgan Chase & Co - Analyst

And maybe just last one, the timelines around this, I think you're going pretty aggressively forward. It sounds like how quickly can you move this through programs?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

We know a lot about how to develop this drug, having done the initial development in atopic dermatitis. We know what kind of patients you should enroll. We -- the FDA is familiar with George's platform. We put more antibodies from a consistent platform, I think, than anybody else in the world. So we know how to get this through. We know how to move it quickly. We know how to identify the right patients, and we're expediting the first one, the IL-13, move very quickly.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

We certainly expect to be competitive with anybody else in the field. And we think that because of our platforms and technologies, these are the best reagents. I mean, we've compared them. They're fully human, they derive, as Len says, from an established platform and they have incredible biophysical properties. I don't think there's better antibodies in the world and the ones that we deliver.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. Maybe just a couple on EYLEA quickly. Now you have RVO and the four-week label enhancements, Talk about what that means for the HD franchise going forward and how we should think about uptake from here?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

So what Chris is referring to, we've got, I would say, two of the three enhancements we'd like, that is to be able to use the drug monthly, if necessary, that's on label, as well as the approval for about 10% to 20% of the market, which is RVO, retinal vein occlusion. Those are very important.

The third leg of that enhancement stool will be, we hope, approved in -- early in the second quarter or sometime in the second quarter, which will be the prefilled syringe.

All of those put together, we have made great progress in getting people to accept that the drug of choice is EYLEA HD. I think it's the only branded product that's actually growing, at least based on last quarter's data. I think that the team is very excited.

We went from about a year ago, a quarter of our franchise sales were in HD to now we're somewhere around 50% and we expect that to keep growing.

Obviously, with competition, biosimilar competition coming for 2 milligrams -- there's some out there already, but more coming later in the year. We're trying to get as much HD traction as we can, and it seems to be going quite well.

We have tried to deal with the foundation issue. This past quarter, we had put up a big match. Nobody had sort of, were willing to go for it. But now in this last quarter, there was a $60 million contribution, which we matched. So that's also going to contribute.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

I think the monthly dosing regimen is actually going to make a big difference because since payers weren't covering monthly dosing, even though only about 5% of patients, because EYLEA HD is so long acting. A very small number of patients need to go to monthly, but physicians were hesitant to start them on something and then have to switch and get approval for a different product. So they weren't starting many patients on Eylea HD.

I think now that they don't have to worry about that, many more will choose what the data says is the best and longest-acting product for most patients.

Christopher Schott - JPMorgan Chase & Co - Analyst

Great. And maybe just one last follow-up on the foundation front. Do we have funding in place at this point to start to reverse some of the biosimilar Avastin dynamics that were playing out last year?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Well, as I said, finally, in the fourth quarter, there was a $60 million contribution, which is a large contribution, which we matched that puts $120 million in there, and hopefully, that will continue.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. Pivoting over to Libtayo. You had your Phase 3 results in adjuvant CSCC were pretty impressive. It seems like KEYTRUDA had some struggles in the same indication. Just what do you think contributed to that difference between what we saw with KEYTRUDA versus what we saw with your drug?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Well, it gets back to the point that I was making about our antibodies for longer-acting IL-13 or 4 or even our next-generation Dupi. A lot of people have the mistaken belief that it's easy to make antibodies and all antibodies are created the same.

I think what the data, if you look at it, as Len said, more fully-human antibodies have been approved from our platform than any other platform, 10% to 20% of all approved antibodies come from our platform. And we repeatedly are producing the best agents with the least number of problems such as ADA, antidrug antibodies, and so forth. And so when you have two antibodies against the same target, they're not necessarily the same. And across many programs.

Remember, other people have tried to make Dupixent like antibodies that all failed, including Amgen. So it's not that easy to always make the best antibodies. Our platform and our people have perfected that ability. And that's why our antibodies seem to work in places where other antibodies against the same targets don't work.

Christopher Schott - JPMorgan Chase & Co - Analyst

So on that commercial opportunity, how big of an opportunity is that incremental indications?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Yeah. I think that could be a blockbuster opportunity in and of itself, probably at least 10,000 people would qualify on label there.

Christopher Schott - JPMorgan Chase & Co - Analyst

Yeah. Excellent. Talking about novel program, you LAG-3, one of the big updates we're waiting for this year. Can you just discuss your confidence in a program here that's going to show differentiation from existing standard of care? I guess, I just -- given the extended timelines here, are you feeling increasingly confident you have a profile that can really separate from Opdualag?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Well, our confidence comes from our previous trials that had showed substantial numbers of patients treated, where it looked like the combination cross study looked better than previous standards of care. Delays in the program have just been because event rates were slower in this trial than we planned or anticipated. That could either be good or bad. We won't know until we unblind the data. But we remain very excited because of the previous trial experience we have with these agents.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

George, were we powered for survival there while others were not?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Yeah. So that's another important point. So in the initial analysis, we'll do our first interim for overall survival, but we are, we believe, adequately or more adequately powered to pick up a survival advantage, even if it was on the order of magnitude of what was seen with the previous LAG-3 combination.

Christopher Schott - JPMorgan Chase & Co - Analyst

And that would, from a market standpoint, really --

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

That would make a difference since they do not have a survival benefit.

Christopher Schott - JPMorgan Chase & Co - Analyst

And just as we frame out this opportunity, can you talk through the size of the opportunity that you would see here in melanoma?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Yeah, it's difficult to quantify, but it is a big -- it is a blockbuster opportunity for sure. We also have the adjuvant melanoma trial, which I guess comes a little bit later. But if you put it all together, our unique data in skin cancer, we were the first, we're the market leader. Our data in adjuvant CSCC, where KEYTRUDA was -- it wasn't like KEYTRUDA was close. KEYTRUDA was a zero, and we were 68% reductions with 'p' point 000 or whatever it was.

So we really, I think, have a big halo effect now going on in the skin cancer, skin oncologist framework. Hopefully, we get some good data out of these two upcoming trials.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. Let's come back to OS. Will we see that OS data with this initial update, or is it independent?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Only if it's positive, but it's probably not powered in the first update, be unlikely.

Christopher Schott - JPMorgan Chase & Co - Analyst

Okay. The other one, I guess, in this indication, non-small cell, how do we think about the decision to go forward there? Is part of this wanting to see some of this melanoma data and how the prop --?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

We want to see the melanoma data, but I think if we had time, we could tell you that, that's far more speculative and risky. And it's not something that we're counting on there.

Christopher Schott - JPMorgan Chase & Co - Analyst

Okay. Adjuvant melanoma. How -- the risk spectrum? How do you see that?

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

More likely than the lung.

Christopher Schott - JPMorgan Chase & Co - Analyst

Okay, perfect.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

So you agree with that, George.

Christopher Schott - JPMorgan Chase & Co - Analyst

Factor XI is going over there. Can you talk maybe first of all, we're going to see some competitive readouts over the next 12 months. How much readthrough should we be thinking about for your programs versus some of the oral data sets we're going to see?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Well, I think there's a big difference between the orals and the antibodies. We can achieve much more specific and complete blockade. They inhibit other proteases, other molecules, and it can't get as deep inhibition as we get. And when you're comparing antibodies, we specifically designed our antibodies.

So one of our antibodies looks biochemically and by all measures to be able to achieve most complete blockade. The other one is designed to get better efficacy by targeting a different aspect of the target. And so I think that having this balanced approach, I think there's actually room for both antibodies, because as I tried to explain, the reason people don't take anticoagulation is because they're afraid of bleeding.

For those people who are most concerned about anticoagulation, we think one of our antibodies may be able to provide them the best efficacy. For those who want to anticoagulate but maybe they want very little, maybe no bleeding risk based on the genetics, our other antibody may be able to provide that. So we may be able to provide exactly what people want. They want to focus on anticoagulation, we'll give you that.

If you're totally worried about bleeding, we may be able to offer you something that will significantly impact your clot risk, but may very much eliminate your fears about bleeding. So we think both of these could be blockbuster opportunities independently. And it's different segments of the population.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

It's worth going back to looking at this slide when you have a chance because on that slide, there's evidence that there's less bleeding in a standard aspirin-induced bleeding with a factor 10 drugs cause increased bleeding and ours doesn't. And there's evidence to better anticoagulation in two settings as well. So we have the preliminary proof-of-concept data. I think it's going to be exciting to see, we probably have a half a dozen Phase III planned.

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

I think that's an important point. A lot of people are very much focused on stroke prevention and atrial fibrillation. We think if you have safer anticoagulants, they can be used much more broadly. So we think, in fact, the other opportunities outside so-called SPAF may end up dwarfing the SPAF opportunity. Everybody is focused on where the puck is now, but with safer anticoagulation, we imagine that the puck may be able to help many, many more people in the future.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. Last few minutes here on me switch over to the C5 program. First, can you talk about MG and just your thoughts of how you see your asset fitting into the broader MG landscape?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Well, I think the thing that's remarkable as we briefly went over. But it seems like in different diseases, you need different degrees of blockade to optimize efficacy, which also allow you to get perhaps even a safer agent out there.

So we showed is that in PNH, you need complete blockade. And there, you need the double combo. What we actually showed that, if anything, something that achieved about in certain assays, about 70% to 75% blockade was the best agent in a side by side to complete blockade but also cross study to every other C5 agent that's been tried out there.

And that might -- it takes a long time to prove it, that might actually come with better safety, which could be an incredible profile. But to remind you, not only do we have the best data compared to C5. But when you look at the other class, the FcRn class of antibodies, those are given in two ways.

If you an optimized safety, they're given for a short period of time and then patients are giving a drug holiday. So you get a U-shaped dose response curve. Essentially, the patients get back their normal level of disease before you retreatment. I'm not sure if that's a desirable profile where your disease is constantly waxing and waning, or you can give lower levels of it for safety reasons, still in the extension studies of those programs, they did also see safety events. But when you give those levels, then you see much less improvement in this famous MG-ADL score.

So we may have an agent that's not only best-in-class among the C5s. May, in the long term, we'll have to prove it to have a better safety profile, but may have better both safety and efficacy profiles compared to the other major competitive class in this area.

So I think it's a very exciting opportunity. And as I said, not only is it an independent opportunity in PNH given in a different way as a combo, but we're exploring it, as Len said, in a variety of ways in geographic atrophy as well. And there could be, once again, we'll see. We like tailored approaches. We like not just trying one thing and hoping it works trying a few different things and see which one works better.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. On that GA program, just your confidence in the approach there and as we approach that data later this year?

George Yancopoulos - Regeneron Pharmaceuticals Inc - President, Chief Scientific Officer, co-Founder, Board co-Chair

Well, the data will speak for itself. We're about six months or a little bit more away from that data. But I think the fact that we think we're going to do at least as well as the existing agents, but perhaps with a better safety profile, at least from the fact of causing occlusive vasculitis in the retina, I think there's reason to be excited about that. So we're very much looking forward to that data.

Christopher Schott - JPMorgan Chase & Co - Analyst

Excellent. Well, I appreciate the update on everything here and exciting year ahead for the company. So thanks again for joining us.

Leonard Schleifer - Regeneron Pharmaceuticals Inc - President, Chief Executive Officer, co-Founder, Board co-Chair

Thank you.
