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REGN.OQ - Q2 2024 Regeneron Pharmaceuticals Inc Earnings Call

EVENT DATE/TIME: AUGUST 01, 2024 / 12:30PM GMT

OVERVIEW:

Company Summary

REFINITIV

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PRESENTATION

Operator

Welcome to the Regeneron Pharmaceuticals second-quarter 2024 earnings conference call. My name is Shannon, and I will be your operator for today's call. (Operator Instructions) Please note that this conference call is being recorded.

I will now turn the call over to Ryan Crowe, Senior Vice President, Investor Relations. You may begin.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thank you, Shannon. Good morning, good afternoon and good evening to everyone listening around the world. Thank you for your interest in Regeneron and welcome to our second quarter 2024 earnings conference call. An archive and transcript of this call will be available on the Regeneron Investor Relations website shortly after the call ends.

Joining me on today's call are Dr. Leonard Schleifer, Board Co-Chair, Co-Founder, President and Chief Executive Officer; Dr. George Yancopoulos, Board Co-Chair, Co-Founder, President and Chief Scientific Officer; Marion McCourt, Executive Vice President of Commercial; and Chris Fenimore, Senior Vice President and Chief Financial Officer. After our prepared remarks, the remaining time will be available for your questions. We anticipate today's call will last approximately 60 minutes.

I would like to remind you that remarks made on today's call may include forward-looking statements about Regeneron. Such statements may include, but are not limited to, those related to Regeneron and its products and business, financial forecast and guidance, development programs

and related anticipated milestones, collaborations, finances, regulatory matters, payer coverage and reimbursement issues, intellectual property, pending litigation and other proceedings and competition. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in that statement.

A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange commission, including its Form 10-Q for the quarter ended June 30, 2024, which was filed with the SEC this morning. Regeneron does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

In addition, please note that GAAP and non-GAAP financial measures will be discussed on today's call. Information regarding our use of non-GAAP financial measures and a reconciliation of those measures to GAAP is available in our quarterly results, press release, and our corporate presentation, both of which can be accessed on the Regeneron Investor Relations website. Once our call concludes, Chris and the Investor Relations team will be available to answer any further questions.

With that, let me turn the call over to our President and Chief Executive Officer, Dr. Leonard Schleifer. Len?

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Thanks, Ryan. Thanks to everyone joining today's call. Regeneron continued its track record of strong execution, highlighted by double-digit revenue and earnings growth in the second quarter along with important advances across our broad pipeline.

For my remarks today, I'd like to briefly review some of the key performance drivers for the quarter and then discuss near-term pipeline opportunities. After my remarks, George will provide further updates on our pipeline. Marion will then review our commercial performance. And finally, Chris will detail our quarterly financial results and discuss updates to our full year guidance.

Second quarter 2024 total revenues grew 12% to $3.55 billion, primarily driven by sales of EYLEA HD in the United States. Higher Sanofi collaboration revenues reflecting the continued strong performance of Dupixent as well as robust growth for Libtayo. EYLEA HD generated $304 million in its third full quarter on the US market and continues to outperform recent launches in the anti-VEGF category. Net product sales for EYLEA HD and EYLEA combined were $1.53 billion, representing a 2.3% growth compared to the prior year.

We are encouraged that despite increased competition in the anti-VEGF space, we have achieved a strong EYLEA HD launch trajectory while maintaining our category-leading combined EYLEA HD and EYLEA market share of 45%. Our efforts to bring an EYLEA HD pre-filled syringe, United States market remain a high priority, and we are tracking towards a potential pre-filled syringe launch by early 2025. In summary, we continue to position EYLEA HD as the new standard-of-care for retinal diseases based on its differentiated clinical profile, coupled with strong familiarity and satisfaction among retinal specialists.

Dupixent global revenues grew 29% on a constant currency basis to $3.56 billion, reflecting strong growth across all approved indications, age groups, and geographies. In June, the European Commission approved Dupixent for COPD in patients with raised blood eosinophils, marking the first global regulatory approval for Dupixent in COPD. This approval enables Dupixent to address the approximately 220,000 eosinophilic COPD patients in the EU that are currently uncontrolled on maximum and eligible therapy. The approval also represents the first biologic approved to treat this disease.

We continue to work with the FDA regarding its ongoing review for this indication and expect their decision by the September 27 PDUFA date. We and our partner, Sanofi, are prepared for US launch that many pulmonologists, respiratory key opinion leaders, and their patients have been eagerly anticipating. There is a high unmet need in COPD with Type 2 inflammation with approximately 300,000 eligible patients in the United States, and our potential launch represents a significant driver for Dupixent's continued growth.

Libtayo global net product sales were $297 million in the second quarter, an increase of 43% on a constant currency basis. Despite intense competition, Libtayo has maintained its leadership position in non-melanoma skin cancers, while making impressive inroads in non-small cell lung

cancer. We are also pleased with the progress we have made in establishing an international commercial footprint to support Libtayo and other future products following our purchase of full global rights to Libtayo from Sanofi in mid-2022.

Regarding linvoseltamab or BCMAxCD3 bispecific for relapsed refractory multiple myeloma. During its review of the linvoseltamab BLA, the FDA informed us that the third-party fill-finish manufacturer for linvoseltamab had unresolved findings from a pre-approval inspection for another company's product candidate.

While we now believe these findings have been resolved, a reinspection will be required and therefore, we anticipate any potential FDA approval for linvoseltamab is likely to be delayed beyond the August 22 PDUFA date. The FDA has not informed us of any approvability issues for linvoseltamab related to safety, efficacy, or the status of our ongoing confirmatory trial. More broadly on our pipeline, we are excited about several upcoming readouts later this year or in 2025 to further inform programs that could support significant long-term growth opportunities which George will discuss in a moment.

In closing, our pipeline continues to generate innovative and differentiated opportunities and now has over 35 programs in clinical development spanning several distinct therapeutic areas. Our commercial team is executing well with our in-market products and is building momentum in competitive categories. Finally, we continue to prudently deploy capital with the goal of delivering long-term value to shareholders.

With that, I'll turn the call over to George.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Thank you, Len. Starting with Dupixent. Regarding COPD, data from our second confirmatory trial, NOTUS, was featured as a late-breaking presentation at the American Thoracic Society Conference and simultaneously published in the New England Journal of Medicine.

In NOTUS, Dupixent reduced exacerbations by 34% while significantly improving lung function, confirming the unprecedented results from the previously reported Phase III BOREAS trial. Based on data from NOTUS and BOREAS, Dupixent was recently approved by the European regulatory authorities for eosinophilic COPD patients uncontrolled on maximum standard-of-care inhaled therapy. Additional submissions are under review with other regulatory authorities around the world, including in the U.S., China, and Japan.

Beyond COPD, later this year, we are looking forward to data readouts from Phase III studies of Dupixent in Chronic Spontaneous Urticaria and Bullous Pemphigoid. Seven years after its initial FDA approval and with approval in seven different indications around the world, Dupixent continues to deliver potential new approvals for additional important disease indications.

Regarding our small pilot study to potentially eliminate severe food allergies using our innovative approach that combines Dupixent and linvoseltamab our BCMAxCD3 bispecific, we continue to expect to see initial data by the end of this year.

On itepekimab, our IL-33 antibody in development for certain COPD patients, our two Phase III studies are now fully enrolled. Study readouts and regulatory submissions for our second therapeutic candidate for this devastating disease are expected in the second half of next year.

Moving to oncology and starting with fianlimab. Our LAG-3 antibody in combination with Libtayo, at the upcoming ESMO meeting in September, we look forward to presenting longer-term follow-up on the metastatic melanoma cohorts from our first-in-human study. Responses have continued to deepen with the proportion of complete responders and median progression-free survival continuing to improve.

These results strengthen our view that fianlimab and Libtayo may be the most promising immunotherapy combination in clinical development. As we recently announced, we are looking forward to the Phase III readout in this melanoma setting next year, which could position fianlimab and Libtayo as a new standard-of-care in melanoma and eventually potentially other cancer settings.

Additionally, we hope to gain insights into the antitumor activity of this combination in non-small cell lung cancer later this year. We are also advancing fianlimab development to earlier lines of therapy with proof-of-concepts in perioperative non-small cell lung cancer and perioperative melanoma now underway with additional indications likely to follow.

On to bispecifics for solid tumors. Our costimulatory bispecific antibodies are being tested in numerous studies, including as monotherapies as well as in combination with CD3 bispecifics and with Libtayo. At the ASCO Conference, we presented results for our EGFRxCD28 bispecific in combination with Libtayo. In microsatellite stable colorectal cancer, tumor historically unresponsive to immunotherapy, EGFRxCD28 in combination with Libtayo demonstrated encouraging antitumor activity, with an overall response rate of 20% in patients without liver metastases. Regarding safety, to-date, we have not observed severe immune-related adverse events with this agent at our recommended Phase II dose. Dose expansion cohorts testing EGFRxCD28 plus Libtayo continue to enroll in various solid tumors, including non-small cell lung cancer with or without EGFR mutations, microsatellite stable colorectal cancer, head and neck, squamous cell carcinoma and others.

On to our PSMAxCD28 costimulatory bispecific, which has already demonstrated promising activity in late-line prostate cancer when combined with Libtayo. We have now initiated combination treatment of our PSMAxCD28 costim bispecific with our PSMAxCD3 bispecific, which based on preclinical studies may maintain the efficacy observed with the Libtayo combination, but may improve the safety and tolerability profile. We are also testing PSMAxCD28 in other cancers.

Next to our bispecifics for hematology oncology. The linvoseltamab, our BCMAxCD3 bispecific, at an oral presentation at the European Hematologic Association Conference, we presented updated pivotal data, which continue to demonstrate a potentially best-in-class profile in late-line myeloma in terms of efficacy, safety, dosing, as well as hospitalization burden. As we expected, responses continue to deepen with longer follow-up. At 14-month median follow-up of 117 patients, 50% achieved a complete response or better with an objective overall response rate of 71%.

Additional studies of linvoseltamab are now also underway in earlier stages of myeloma and in precursor conditions such as smoldering myeloma and monoclonal gammopathy of unknown significance or MGUS. Developing linvoseltamab in earlier-line myeloma settings presents an important opportunity for us to help patients and their physicians in these diseases, which currently have complex treatment paradigms.

Touching on our non-oncology hematology pipeline. As highlighted previously, later this year, we are anticipating proof-of-concept results for our two Factor XI antibodies in the setting of prevention of venous thromboembolism after knee replacement surgery. The study for the antibody targeting the Factor XI A2 domain is now fully enrolled, and we expect to present results at a medical meeting in the second half of this year.

Interim Phase II results for our second Factor XI antibody, which targets the catalytic domain, are expected by the end of this year for internal analysis. We have also started an additional proof-of-concept study to further evaluate the two antibodies' profile for thrombosis prevention in patients who have a peripherally inserted catheter. Results of these studies will inform whether to proceed to registrational studies with one or both of these antibodies by next year.

Moving to obesity. Our most advanced approach is designed to address the potential negative consequences of widespread use of GLP and GIP receptor agonists. As has been widely reported, the profound weight loss caused by these agents, unfortunately, can also result in substantial loss of muscle, which is particularly concerning in older obese patients. Our myostatin antibody when combined with semaglutide with or without our activin-A antibody may protect against this muscle loss, as previously demonstrated in non-human primates.

Part A of our COURAGE Phase II study testing a higher dose of trevogrumab, our myostatin antibody, in healthy subjects has now been successfully completed with no new safety signals identified. Part B of the study, which evaluates our muscle preservation antibodies in combination with semaglutide in obese participants has started enrolling patients. Assuming a reasonable pace of enrollment, we continue to expect to report top-line results, including changes in body weight, fat mass and muscle mass, by the second half of 2025.

I will conclude with our genetics medicines efforts. At the ASGCT Conference, we presented updated data from our DB-OTO gene therapy program for genetic hearing loss due to mutations of the otoferlin gene. The first child treated with this therapy, an 11-month-old girl who was profoundly deaf at baseline, had hearing in the normal range by 24 weeks after treatment. Also, initial hearing improvements were observed in a second child, dosed at 4 years of age, at a 6-week assessment with additional follow-up planned.

As of July, we have dosed five patients in our study, and we are on track to enroll several more patients this year. We also look forward to bringing additional otoferlin gene therapy programs to the clinic in the coming years with the potential to address more common forms of monogenic hearing loss.

Regarding our Intellia collaboration in transthyretin amyloidosis with cardiomyopathy… the world's first Phase III program for an in vivo CRISPR-based therapy is enrolling at a rapid pace, indicating considerable interest from investigators and patients. In addition, we are also on track to be the first to use of CRISPR technology to insert a corrective gene in vivo for a deficiency disease, hemophilia B. As noted previously, we have enrolled initial patients in the leading portion of this trial, and first patient should be dosed soon.

Our siRNA collaboration with Alnylam has not only demonstrated successful silencing of genes in the liver, but also for the first time for siRNA in the brain. This opens up opportunities for us to go after other disease-causing genes in the brain.

A study of ALN-SOD in ALS patients with SOD1 mutations recently initiated. Other CNS-directed siRNA programs are expected to enter the clinic shortly, including targeting HTT for Huntington's disease, synuclein for Parkinson's and tau for Alzheimer's and other neurodegenerative diseases.

Additionally, with regard to our C5 program… our innovative approach involving the first combination of an antibody together with an siRNA both targeting the same molecule is progressing well and we are expecting to present updated data for our initial potential indication, paroxysmal nocturnal hemoglobinuria, by the end of this year. We're also looking forward to starting our Phase III program in geographic atrophy in the second half of this year.

In summary, we continue to drive forward our innovative development pipeline and anticipate reading out several pivotal and proof-of-concept data sets over the next 12 to 18 months. Our early research efforts continue to be productive, with multiple novel programs potentially advancing to the clinic over that same time frame.

And with that, I will turn the call over to Marion.

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

Thank you, George. Our second quarter commercial results further solidify Regeneron's leadership across therapeutic categories. Our performance demonstrates the ongoing strength and diversity of our product portfolio with continued growth opportunities powered by existing and upcoming product and indication launches across multiple geographies.

I'll start with EYLEA HD and EYLEA in the US. In the second quarter, combined net sales for both medicines grew 2.3% year-over-year to $1.53 billion. EYLEA continues its clear category leadership while EYLEA HD remained the fastest growing medicine in this highly competitive category. EYLEA HD continued its launch momentum in the second quarter, delivering net product sales of $304 million, which represents 52% sequential growth. EYLEA HD continues to be the fastest launch of any anti-VEGF therapy since EYLEA more than a decade ago, and the trajectory confirms a significant transition to EYLEA HD is underway.

The breadth and depth of EYLEA HD prescribing continues to grow with utilization across a broad range of patients, including the treatment-naive population, which has doubled since last quarter. Physicians are also increasingly switching patients to EYLEA HD from other anti-VEGF treatments based on their positive early treatment experiences.

In these switch patients, early real-world data indicate that treatment intervals are being extended with EYLEA HD. EYLEA HD's durability, along with the same trusted efficacy, visual acuity and safety as EYLEA, represents a meaningful improvement for patient lives and greater efficiency for physician practices.

The number of physician offices ordering EYLEA HD during the second quarter increased by more than 50% compared to the prior quarter. We believe this suggests prescriber confidence in EYLEA HD's clinical profile as well as in reimbursement now that the permanent J-code has been well established.

Of note, we recognize the importance of providing physicians with a pre-filled syringe option, and as Len mentioned, we're excited about our anticipated EYLEA HD pre-filled syringe launch. In summary, we're pleased with our second quarter performance for EYLEA HD and EYLEA and remain on track to achieve our goal of establishing EYLEA HD as the new standard-of-care for retinal disease.

Next to Dupixent, which delivered 29% growth in the second quarter on a constant currency basis with global net sales of $3.56 billion. We are approaching the important milestone of 1 million patients on Dupixent worldwide. In addition, there is substantial opportunity for even more patients to benefit from Dupixent based on significant unmet need across indications, ages and geographies.

In the US, net sales grew 24% to $2.61 billion, driven by an increased demand across all five approved indications. Dupixent continues its number one leadership position and new-to-brand prescriptions across all approved indications. Our commercial team remains laser-focused on pursuing initiatives that drive patient awareness and support prescribing. We continue to see increasing penetration in our blockbuster indications of atopic dermatitis, asthma and nasal polyps.

Additionally, recent launches in eosinophilic esophagitis and prurigo nodularis are exceeding our expectations and new patient initiations are steadily increasing. We hear remarkable stories of patients as young as one year of age with EoE, who are now thriving on Dupixent following its approval in January of this year.

The European Commission also recently approved Dupixent in COPD patients with raised blood eosinophils, with patients already getting treatment in Germany. We all recognize that there is significant unmet need worldwide among patients with this debilitating disease and Dupixent represents the first biologic medicine for COPD. Our US team is ready for the anticipated FDA approval of Dupixent in COPD by late September and estimate approximately 300,000 US patients may benefit from Dupixent in this indication. Separately, an FDA decision for Dupixent in adolescents with chronic rhinosinusitis and nasal polyps is expected next month.

As George mentioned, there are two Dupixent Phase III programs reading out later this year, in chronic spontaneous urticaria and bullous pemphigoid. If data from these trials are positive, Dupixent has the potential to support even more patients with unmet need.

We also made significant progress with Libtayo in the second quarter with global net sales of $297 million, up 43% year-over-year on a constant currency basis. Strong commercial execution resulted in market share gains across both skin and lung cancers.

In the US, net sales grew 40% to $182 million with growth across all market segments and indications. In non-melanoma skin cancer, we continue to extend Libtayo leadership with increasing demand and market share. In lung cancer, Libtayo is recognized by physicians as an important therapy for their lung cancer patients and continues to gradually gain market share. Outside the US, our teams are delivering excellent results with net product sales of $115 million as Regeneron continues its international expansion. Libtayo net product sales in some of these international markets were favorably impacted by approximately $15 million of stocking purchases.

Our oncology team is also eagerly awaiting the potential FDA and EU decisions for linvoseltamab in late-stage myeloma. We believe linvoseltamab represents the best-in-class opportunity, and we look forward to potential launch.

In summary, our commercial team continues to deliver on our goal to provide Regeneron medicines to even more patients worldwide. There is meaningful future growth potential within our approved indications and our robust pipeline provides both near and long-term opportunities to advance patient care.

With that, I'll turn the call over to Chris.

Christopher Fenimore - *Regeneron Pharmaceuticals Inc - Chief Financial Officer, Senior Vice President - Finance*

Thank you, Marion. My comments today on Regeneron's financial results and outlook will be on a non-GAAP basis unless otherwise noted. Regeneron delivered strong double-digit top and bottom-line growth in the second quarter.

Total revenues increased 12% year-over-year to $3.5 billion, primarily driven by strong execution of the ongoing EYLEA HD launch in the US, higher Sanofi collaboration revenue and continued global sales growth from Libtayo. Second quarter diluted net income per share grew 13% from the prior year to $11.56 on net income of $1.4 billion. Second quarter revenues from our Sanofi collaboration grew to $1.1 billion, primarily composed of our share of collaboration profits of $988 million, which increased by 32% compared to the prior year, driven by Dupixent's continued volume growth and improving margins.

Reimbursement from manufacturing and commercial supply, the other component of Sanofi collaboration revenue, was $157 million. Taking into account increased volumes, offset by manufacturing efficiencies, we continue to expect reimbursement for manufacturing and commercial supply in 2024 to be comparable to 2023 on a full year basis. The Sanofi development balance was approximately $2 billion at the end of the second quarter, reflecting a reduction of approximately $190 million from the end of the first quarter. We continue to anticipate this balance will be fully reimbursed to Sanofi by the end of 2026.

Moving to Bayer. Second quarter ex-US net sales of EYLEA and EYLEA 8 mg were $908 million, up 8% on a constant currency basis versus the prior year. Total Bayer collaboration revenue was $375 million, of which $353 million related to our share of net profits outside the US.

Now to our operating expenses. Second quarter R&D expense grew 10% year-over-year to $1.1 billion, reflecting continued investments to support our robust pipeline, including late-stage oncology and hematology programs. We continue to make thoughtful investments to enable us to move quickly into Phase III programs if supported by data readouts anticipated over the next 12 to 18 months.

SG&A grew 19% from the prior year to $666 [$667] million in the second quarter, primarily driven by investment to support the launch of EYLEA HD as well as our ongoing international commercial expansion. Second quarter gross margin and net product sales was approximately 89%, which reflected ongoing start-up costs for our fill/finish manufacturing facility.

Now to cash flow and the balance sheet. Regeneron generated approximately $1.6 billion in free cash flow through the first six months of 2024 and ended the quarter with cash and marketable securities less debt of approximately $14.8 billion. We repurchased approximately $900 million of our shares through the first six months of the year and had approximately $3.6 billion available for repurchases as of the end of the second quarter.

Finally, we have made some minor changes to our full year 2024 financial guidance. We have updated our 2024 gross margin guidance and now expect gross margin to be approximately 89%, primarily reflecting anticipated changes in product mix as well as higher non-product specific costs, including start-up costs for our fill/finish facility. A complete summary of our latest full year guidance is available in our press release issued earlier this morning. In summary, Regeneron delivered outstanding results in the second quarter and is well positioned to continue to drive growth in the near and long-term.

With that, I'll pass the call back to Ryan.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thank you, Chris. This concludes our prepared remarks. We will now open the call for Q&A. To ensure we are able to address as many questions as possible, we will answer one question from each caller before moving to the next. Shannon, can we go to the first question, please?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Tyler Van Buren, TD Cowen.

Tyler Van Buren - *TD Cowen - Analyst*

Hey, guys. Good morning. Congratulations on the great quarter. Regarding the EYLEA franchise, I'm really encouraged to see that the overall franchise is up year-over-year and that the 45% category share is maintained quarter-over-quarter. So do you believe that EYLEA HD is reaching a stage and maturity of its launch, where it will allow the overall category share to be relatively stable in the coming quarters that will allow you to participate in the retinal disease market growth and is the market still growing around 10% year-over-year?

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

So Tyler, I'll take it in a couple of pieces. Thank you for the question. First, I did want to comment, we were very pleased to report the total net sales of 1.4 -- excuse me, $1.54 billion in the quarter. Obviously, as you mentioned, that's a 2.4% increase year-over-year.

Additionally, I'll just comment a little bit more on EYLEA HD. We certainly are very much in the launch stage. This is our third full quarter of results that we're reporting today. And certainly, we're encouraged that in the quarter, we had a 52% increase in net sales. And certainly, that calculation represents a $100 million net sales increase from the prior quarter, which is very significant in this competitive market.

So certainly, we are continuing to progress our launch and see it as important. Certainly, EYLEA is an important source of switch patients for EYLEA HD. Next, we see switches coming from faricimab, also Avastin, very pleased as well this quarter to report that we're seeing increased use of EYLEA HD in naive patient population. So all-in-all, we see this indicative that EYLEA HD has the potential, and certainly the profile to be the new standard-of-care.

I think you also asked me about market growth, overall market growth. Let me cover that as well. I would say probably at this stage in the year, we're tracking more on single-digit growth in the category in the midrange, as opposed to double-digit, which I think is what was cited in your question.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

That's right. Okay. Thank you, Marion. Let's move to the next question please.

Operator

Evan Seigerman, BMO Capital Markets.

Evan Seigerman - *BMO Capital Markets - Analyst*

Hi, guys. Thank you so much for taking my question and always congrats on the progress. I want to touch on your work in obesity specifically with leptin. Can you just walk me through some of the rationale of moving this to a Phase II? I know that leptin had been controversial. Clearly, you saw some interesting data in earlier trials. But why do you want to add this on top of say, tirzepatide, versus using triple agonist that Lilly is doing some of the other trials. Thank you so much.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Well, we have leptin going forward in a number of different programs. I believe the one that you're talking about is in combination with other weight loss agent. And that's based on results that suggest that, the reason leptin doesn't work in normal obese patients is because in those patients

who have a high degree of fat and are, in fact, on the upswing of their obesity profile, their leptin levels are very high. They're already saturating. Once you undergo profound weight loss, the leptin levels drop, and you may be getting into the range where the leptin is now providing a signal, which is creating an increased desire in the individual to eat. And so in these patients, it may be that some of the weight loss is limited by decreases in the leptin, which is then driving increasing feeding type of behavior.

So this might be, and at least it's been shown in animal studies to be, the situation where leptin might actually be playing an important role. So as you point out, in historical studies in stably obese patients, leptin is already saturated and giving more leptin may not have a benefit. But in these settings where there are falling leptin levels, the falling and low leptin levels may lead to a food-seeking drive and giving leptin in that setting may allow further weight loss on top of that obtained with these other agents, which tend to plateau at a certain point, and that plateau at least based on animal studies may be in part driven by these drops in the leptin. And these studies, as you know, are done in collaboration with a partnership with Lilly. So we're studying it in collaboration with their agent tirzepatide.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, George. Let's move to the next question.

Operator

Brian Abrahams, RBC Capital Markets.

Brian Abrahams - *RBC Capital Markets - Analyst*

Hey, good morning. Thanks for taking my question and congratulations on the quarter and all the progress. On linvo, as you prepare for the potential launch there, I'm curious the feedback you're getting on how docs may position it relative to existing therapies, how much appreciation there is out there for the efficacy and administration advantages that you cited in your slide? And maybe you could also elaborate a little bit more on some of the issues with the third-party facility and [if] they're confident if that's resolved. Thanks.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

I'll take the third-party issue and George can cover, or Marion, how people are thinking about a BCMA approach and where it might fit in the longer term. There's been a lot of third-party filler type and manufacturing issues with lots of CRLs across the biopharmaceutical space.

As you know, we had one last year with HD EYLEA... And this was a case where the FDA was inspecting our filler for a different product. And they found some observations, the observations needed to be remediated, but because of the nature of the observations, a reinspection is necessary. We believe, based on what we've been told, is that the observations have been remediated. But since there's a reinspection required, it might not get done, it's likely not to get done in time for our PDUFA date. That's why we called your attention to that.

This is an industry-wide issue. I think the FDA is, in fact, planning some public hearing on these sorts of things. We're working with the FDA because this is a priority review application, to see how we can resolve this in as expeditious manner as possible.

George or Marion, do you want to cover these?

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Yes, I'll start and then I'll hand it over to Marion. But as we summarized and we've detailed and as it will continue to be presented, the efficacy data with our bispecific continues to look like it is leading the field as the data matures, and patients continue on treatment, they continue to progress to deeper and deeper responses and where now we have complete response rates at 50% with, we believe, best-in-class PFS and overall survival type numbers.

This is obviously really important because what cancer treatment is all about is trying to eliminate the cancer and getting long-term durable responses and survival in the patients. And we would imagine that this is exactly what patients and physicians are focused about. Other aspects of our profile, we also believe in terms of safety and our dosing schedule and hospitalization burden also, we believe, are best-in-class. In terms of how Marion believes the physician community is appreciating the data, I'll ask Marion to comment on that.

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

Thanks, George. And certainly, we're very excited about the potential upcoming approval for linvoseltamab. George describes the differentiated clinical efficacy, safety profile that will be incredibly important to physicians. We have a highly experienced hematology team in place and ready for launch.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Yes, I would just add, this is Len. I would just add that we're not limiting ourselves, obviously, just to the last line. We are trying to move this aggressively either in monotherapy or in combinations to much earlier lines of therapy.

The rule of thumb has been in cancer that you tend to get more responses as you move to earlier lines. But this would be quite remarkable given what George just told you about the amount of responses we're seeing in the last line. So we're very excited about moving this forward and we'll keep you updated as we do that.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Yes. Just a follow-up on what Len said, obviously, this is why we're moving to these trials in these earlier lines of therapy. Obviously, we won't be commercializing in those areas until we get the results from those clinical trial.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Sure. Absolutely.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

All right, gentlemen. Let's go to the next question.

Operator

Cory Kasimov, Evercore ISI.

Cory Kasimov - *Evercore ISI - Analyst*

Thank you, guys. Good morning. Thanks for taking the question. So we're getting an increasing amount of inbound interest in your Factor XI program. Can you speak to the differences, I guess, probably for George, between your two antibodies? And what will be the key aspects you'll be focused on in your upcoming readouts to know you're on the right track? Thank you.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Yes. So very importantly, what we've done is we've created antibodies that split the mechanism of action. One affects the activation domain, the other the catalytic domain. We have developed in both these classes, the only ones in class or the best-in-class type of antibodies, which are best at actually hitting and inhibiting that target. Based on all of the science, a huge amount of genetics, in part fortified by our own Regeneron genetics efforts and so forth, it suggests that these two approaches will allow us to separate and optimize optimum efficacy and optimum safety.

So it's quite possible that we might actually move forward with both of these antibodies for different target populations, in some of which where efficacy is the primary driver, and others where safety might be most important. So they're very unique in their mechanisms of action. They really are exploring this target both much more precisely by splitting the mechanism of action, but also more powerfully than competitors that have antibodies that can do one or the other of these things.

So we're very excited about these programs. As we said, we have some proof-of-concept studies ongoing, and we hope by the end of the year to be able to announce the directions we may be taking either or both of these antibodies going forward in the future.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, George. Let's move to the next question, please, Shannon.

Operator

Chris Raymond, Piper Sandler.

Christopher Raymond - *Piper Sandler - Analyst*

Hey, thanks. And just a quick question on EYLEA and the commercial progress. So you guys, I think, were pretty clear in your messaging on the permanent J-code is we should not really see an inflection that was seen maybe with VABYSMO when they got their permanent J-code as there were some other variables such as discounting, et cetera, going on with that example.

But we've gotten some market feedback that access barriers remain even with the J-code change and specifically among Medicare Advantage plans. Marion, I'm curious if you can talk about the dynamic there and how you see things playing out with respect to access post permanent J-code.

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

Sure. I'm very, very happy to comment. So certainly, for a portion of the market, fee-for-service Medicare patients, there's open access and freedom of prescribing for physicians. If we go to those areas of the market where there's a payer impact, our teams have successfully opened access for EYLEA HD in a way that covers over 80% of patient lives.

So certainly, significant progress has been made and we continue to work through situations where physicians might be having some utilization management or step edits. I will share that those are often easily managed when the physician and office staff provide information. But overall, the takeaway message should be that EYLEA HD has a very strong payer coverage. And again 80% of the market where reimbursement is in place.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, Marion. Let's move to the next question, Shannon.

Operator

Akash Tewari, Jefferies

Unidentified Participant

Hi. This is Kathy on for Akash. So for your myostatin program, can you talk about your preference for using a doublet versus triplet combination approach in your Phase III trials? And also where do you think myostatin will stack up versus GIP/GLP/amylin combination approaches, which could show potentially like 90% plus fat versus muscle loss. Thank you.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Yes. Well, once again, what we focused on is creating individual reagents that allow us to best dissect the pathway and separate out which are the most important players. As you're aware, other people, for example, are using an antibody that blocks all the pathways, not only the two that we've targeted, but about 20 others that are irrelevant for muscle and are known to have a variety of other potential side effects and adverse effects.

So we targeted the two muscle-specific pathways in this whole mechanism. And what we want to see is which one might have the best efficacy to safety profile. That we believe is very important. Once we determine that, we may move forward with either one or both of these antibodies in combination with the weight loss agents, or we also have been developing in our pipeline, a variety of unimolecular solutions that will allow a single molecule to do whichever one of these multiple pathways we want to attack in addition to the weight loss pathway.

So what we're hoping to do, is by dissecting the pathway as precisely and scientifically as possible, allow us to choose between the unimolecular solutions that we can have to follow on. That said, remember, it's not just a matter of amplifying the weight loss because, with more weight loss, regardless of pathway you use; you can throw on the GLP-1 agonist, you can throw on GPR antagonist, you can lay on additional pathways. The more weight loss and the more rapidly it occurs, which is what patients want, out of necessity, because you're mimicking the starvation cachectic pathway, it inevitably leads to muscle loss, because of activation of these very pathways that we're looking at.

So any approach right now that focuses on rapidly causing weight loss will of necessity, because it plugs into evolutionarily conserved pathways, result in profound lean body and muscle loss, which can be a huge detriment to these patients, especially the older obese patient. And by invoking these agents blocking these specific pathways, we may be able to do two things. We may block this associated necessarily evolutionary conserved muscle loss that accompanies rapid and profound weight loss, while also perhaps increasing the amount of fat loss, which is what you specifically want to lose.

This is what we've now shown in preclinical studies, including through nonhuman primates and these studies that we're embarking on right now should tell us whether all of these pathways, which are incredibly evolutionarily conserved, will indeed pertain in humans and whether we really can optimize not only the weight loss, that's not what's important, but optimize particularly fat loss while maintaining the muscle. And we believe we're the only ones who are properly precisely interrogating the pathways and we'll be able to dissect them to decide on which exactly is the best, safest pathway to give the best benefit to the patient.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Okay. Thanks, George. Shannon, next question, please.

Operator

Chris Schott, JPMorgan

Christopher Schott - *JPMorgan - Analyst*

Great. Thanks so much for the question. Just on linvo, Dupixent and food allergy. I know it's early, but an exciting program. Can you help us just a bit to frame out the number of patients or percent of those with food allergy where you think this could be an appropriate treatment if the data we see later this year and going forward supports moving that combination forward? Thanks so much.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

I think that it's all going to be a matter of the benefit to risk profile once again. And this is what, as I've said in these other programs we're focusing on. We believe, based on all the data that we've shown, that we may have a very safe way of eliminating the actual cells that are causing all these allergic responses, and then very safely keep them from coming back by giving one of the world's historically most safe biologics, which is Dupixent. Of course, we have to prove this in patients.

And so we are starting in the most severe food allergy patients. And in these patients where they have, for example, very high unmet need, very high risks and so forth, it warrants undertaking this approach. The more effective it is, but more importantly, the safer we can prove it is, then the broader the population can go. And in fact, if ultimately, we really have a very safe way of eliminating all allergy inducing cells and then preventing their rebound.

And remember, particularly, most of these patients are also suffering from other allergic diseases, some of them may already be indicated for Dupixent. So you're giving them a drug which may actually be helping them anyway and has been shown to be quite safe in terms of as almost any biologic goes. We may be able to go into milder and milder allergy patients. So we can start and we are starting with the most severe patients. We're seeing in these patients with a high unmet need, whether this approach is both effective, but also safe and how safe it is, and the safer it is, we can broaden wider and wider.

There's also ultimately no need to be limited to food allergies, you can actually eliminate essentially all allergies from the most serious to the most mundane, but it depends on the benefit risk and the safety, which is what we're testing in these initial studies. And for the initial studies, we're taking the most severe food-allergic patients who have a very high unmet need and very high-risk profile. Depending on how it goes there, we can broaden to milder and milder types of disease.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

I mean the numbers get quite staggering. Looking at -- if you just look at the number of emergency room visits a year, it could be hundreds of thousands of millions of people go to the emergency room for food-based allergies. Obviously, a smaller number for actual anaphylaxis.

But just to reinforce exactly what George says, if all it takes is an induction in BCMA to induce the process where you can get on to Dupi, Dupi is a very safe agent, and we've got hundreds of thousands, approaching million of patients on the drug. So we know the profile of that drug. So this all makes great scientific sense. We just have to take our time, do it safely and see how it develops.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, Len and George. Let's move to the next question, please.

Operator

Tim Anderson, Wolfe Research.

Tim Anderson - *Wolfe Research - Analyst*

Thank you very much. I have a question on EYLEA and this DOJ investigation into the marketing practices that emerged since April, where they assert that you guys violate the False Claims Act. Can you provide an update on what happens from here, specifically in the interim and out of prudence, has Regeneron changed any of its marketing practices since April? And is that having any impact even on prescribers? I asked because on Slide 6, you mentioned, other market dynamics that resulted in lower volumes and lower price. I am just wondering what those were.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

There's nothing in the marketplace related to this lawsuit. And frankly we think there's nothing to this lawsuit. And we have not changed our practice, and we intend to fight it vigorously. And I think once you see our papers in court, you'll get a much better understanding of that.

Operator

David Risinger, Leerink Partners

David Risinger - *Leerink Partners - Analyst*

Yes. Thanks very much. So Regeneron is obviously a tremendous R&D leader, but there's also substantial innovation happening outside of the company, and the company has a tremendous balance sheet that it's not really putting to work. So my question is, is there an opportunity to leverage Regeneron's eye disease commercial presence by acquiring novel potential blockbuster therapies for severe eye disease. And if so, does the company see any opportunities in the near to medium term to do so? Thanks very much.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Yes, it's a great question, and it's one we ask every day here. Is there some opportunity that isn't resulting from our own innovation that we should be trying to acquire. We have not seen any such, large scale. Obviously, we've done some smaller scale and hundreds of millions of kind of numbers or a few million and whether or not we would -- we could leverage any of our in-line products or research capabilities, it's certainly something we think about, but there's nothing that we at the moment, for late-stage products, see an opportunity for.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, Len. Let's move to the next question, please, Shannon.

Operator

Salveen Richter, Goldman Sachs.

Salveen Richter - *Goldman Sachs - Analyst*

Good morning. Thanks for taking my question. On the Factor XI programs here, could you speak to the potential commercial opportunities that are represented and what the future development plans look like here? Thank you.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

Well, as I said, we're in the stages of evaluating our Factor XI two classes of antibodies that are attacking this pathway in two different ways. We expect I think we've already talked about: One of them will be more effective at preventing clot formation, but potentially come with slightly more serious side effect profiles. The other might be less effective, but much safer.

And as I said, we thought it was important to really precisely interrogate this pathway using these two antibodies that are attacking two different parts. So this is one enzyme; it has an activation domain, a catalytic domain. And by blocking independently the two different domains, we expect to deliver two different profiles each one with the best-in-class antibody.

Once we really understand those profiles, we will understand in which directions to be taking either one, or both potentially, of the antibodies. We can easily imagine taking forward, the more effective one, but for a higher-risk patients, let's say, the less effective one into settings where you might want more safety and clot prevention is not as important. So all of this is going to depend on these profiles.

And as I said, we hope to get our key data by the end of this year, and that should better define the efficacy and safety profile, how they compare to the various existing agents that are out there now, and which direction to take them for which indication. So two antibodies, two distinct profiles, we hope to better understand them based on our initial proof-of-concept study.

And from there, we'll understand where to take them and what the ultimate opportunity will be. But obviously there's still enormous need here for agents that can block clot and thrombus formation. And so much depends on safety profiles here, and we're very excited about having the opportunity to have these two very related, but distinct profiles.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Just to amplify a little bit of what George said the direct oral anticoagulant market is a very, very large market. It's about a $20 billion market. if you could bring to part of that market, most of that market, or some fragment, similar efficacy, but with a better safety profile, then you really have a big opportunity here. So that's what we're focusing on.

Can we deliver with one or the other antibody in the proper setting, as George was suggesting, a same or better efficacy, but with a better safety profile. If we can give you that, if we can give patients that, then we will be able to really have a big, large market opportunity.

George Yancopoulos - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Scientific Officer*

And there are many settings where you don't use certain agents because of the safety profile, which could create whole new opportunities as well.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Okay. Thank you. Let's move to the next question please, Shannon.

Operator

Carter Gould, Barclays

Carter Gould - *Barclays - Analyst*

Good morning. Congrats on the quarter. I appreciated the earlier commentary from Len on the pre-filled syringe effort, I guess, but for Marion and the team, just the confidence that the high dose launch momentum won't be disrupted by the relative near-term disadvantage of VABYSMO having a pre-filled syringe and if you wanted to give more specificity on your own timelines, that would be appreciated. Thank you.

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

Well, I think I said in my prepared remarks that we're anticipating a launch in early 2025. I'm not sure what the competition is actually going to do about launching, but we're a matter of months, I think, apart if they launch ahead of us. And so I don't think that that's going to have a significant impact in the marketplace. Where people really are focused, I think, is on the profile of our drug, the durability of our drug, the safety experience they've had with aflibercept, the active ingredient... So we feel pretty confident in the ongoing launch.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thank you. We have time for two more questions, please, Shannon.

Operator

Terence Flynn, Morgan Stanley.

Unidentified Participant

Hi. This is Chris on for Terence. Just one question from us about EYLEA HD. Given what you have seen in the market dynamics in 2Q, how should we think about the pace of conversion for the second half of 2024?

Leonard Schleifer - *Regeneron Pharmaceuticals Inc - Co-Chairman of the Board, President, Chief Executive Officer, Founder*

You should think hard about it. That's your job. I don't know if Marion wants to have any comment there.

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

I would just say that as I commented earlier, we're very pleased in our progress in the EYLEA HD launch.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

All right. Thank you. Let's move to the final question, please, Shannon.

Operator

Mohit Bansal, Wells Fargo

Mohit Bansal - *Wells Fargo - Analyst*

Thank you very much for taking my question. I just want to, again, talk about EYLEA HD. In terms of -- Marion, if you could comment on, at this point, how much is switch versus naive patient adjustment? I assume most of them are switch, and are they difficult-to-treat patients in the beginning?

And then when you think about going forward, do you think you're in the early innings of conversion? Or do you think there is some other dynamics we should think about from the pricing as well as access point of view as we model EYLEA HD versus standard dose EYLEA going forward? Thank you.

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

So it's always a combination of initiation for EYLEA HD of switch patients and then, of course, naive patients. So, I mentioned the profile today of switch patients to EYLEA HD, which is very encouraging, comes not surprisingly from EYLEA because it's the largest product in the category, secondarily from faricimab, and then the third source of switch patients would be Avastin, and then there's everything else. But what's really encouraging, as I mentioned in the quarter, is that the utilization among treatment-naive patients doubled from the prior quarter. So we'll continue to see an ongoing combination as does every product potentially, if it's got the right profile in the category, but the evolution of prescribing to EYLEA HD is progressing very well.

Ryan Crowe - *Regeneron Pharmaceuticals Inc - Senior Vice President, Investor Relations & Strategic Analysis*

Thanks, Marion, and thanks to everyone who dialed in today for your interest in Regeneron. We apologize to those remaining in the Q&A queue that did not have a chance -- that we did not have a chance to hear from. As always, the IR team is available to answer any remaining questions that you may have. Thank you once again and have a great day.

Operator

This concludes today's conference call. Thank you for your participation. You may now disconnect.
