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EDITED TRANSCRIPT

REGN.OQ - Q2 2023 Regeneron Pharmaceuticals Inc Earnings Call

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OVERVIEW:

REGN reported 2Q23 total revenues of $3.2b, non-GAAP net income of $1.2b and non-GAAP diluted EPS of $10.24.

REFINITIV

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PRESENTATION

Operator

Welcome to the Regeneron Pharmaceuticals Second Quarter 2023 Earnings Conference Call. My name is Shannon, and I will be your operator for today's call. (Operator Instructions) Please note that this conference is being recorded. I will now turn the call over to Ryan Crowe, Vice President, Investor Relations. You may begin.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - VP of IR

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 2023 earnings conference call.

An archive of this webcast will be available on our 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 and Head of Commercial; and Bob Landry, Executive Vice President and Chief Financial Officer. After our prepared remarks, we will open the call for Q&A.

I would like to remind you that remarks made on today's call may include forward-looking statements of Regeneron. Such statements may include, but are not limited to, those related to Regeneron and its products and business, financial forecast and guidance, revenue diversification, development programs and related anticipated milestones including anticipated regulatory actions, 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 quarterly period ended June 30, 2023, 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 measures will be discussed in today's call. Information regarding our use of non-GAAP financial measures and a reconciliation of those measures to GAAP is available in our financial results press release and our corporate presentation, which can be accessed on our website. Once our call concludes. Bob Landry and the IR team will be available to answer further questions. With that, let me turn the call over to our President and Chief Executive Officer, Dr. Len Schleifer. Len?

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

Thanks, Ryan, and thanks to everyone joining today's call. Regeneron delivered strong results across the organization in the second quarter of 2023 while continuing to make progress toward our long-term objective of growing the business while simultaneously diversifying its revenue and earnings streams.

Total revenues increased by 11% compared to the prior year quarter, primarily driven by Sanofi collaboration revenues and Libtayo net product sales, which grew by 39% and 49%, respectively.

Non-EYLEA revenue contributions were 41% of total revenues. The highest proportion for any quarter in the last 10 years, excluding those with COVID antibody revenue contributions. Overall, we were pleased with the trajectory of the business and believe the company continues to be well positioned to deliver long-term growth.

In a few minutes, George, Marion and Bob will provide commentary on pipeline developments, commercial execution and financial results that we achieved during the second quarter. For the remainder of my remarks today, I will focus on aflibercept 8 milligrams.

We are very excited about the emerging clinical profile including the compelling 2-year data from the pivotal PHOTON study in patients with diabetic macular edema, which George will discuss in more detail.

Now I will summarize the progress that has been made toward getting this important product candidate approved by the FDA. As we announced in late June, the Complete Response Letter, or CRL, that we received from the FDA regarding our biologic license application for aflibercept 8 milligrams for the treatment of patients with wet age-related macular degeneration, DME and diabetic retinopathy did not identify any issues related to aflibercept 8 milligrams clinical efficacy, safety profile, trial design, labeling or drug substance manufacturing nor has the FDA requested any additional clinical data.

The CRL was entirely based on unresolved observations resulting from the May 2023 FDA pre-approval inspection of a third-party contract manufacturing organization, Catalent that we generally engaged to complete vial filling for aflibercept 8 milligrams. The inspection observations were noted in a Form 483 and were related to a manufacturing line in Catalent's facility that is used to fill vials with aflibercept 8 milligrams as well as our C5 antibody, pozelimab, for the ultrarare CHAPLE disease, which has a PDUFA date of August 20.

The inspection was conducted as part of the FDA review process for both the aflibercept 8-milligram BLA and the pozelimab BLA. Broadly speaking, the observations cited production and process control procedures, equipment validation and facility maintenance.

We, Catalent and the FDA have had multiple discussions since the aflibercept 8-milligram CRL. There is a clear understanding of the remediation work that is required to allow the FDA to resume approving BLAs that involve manufacturing on this line. Catalent has already provided data and information to the FDA that could satisfy some of these requirements and expects to be able to provide the remaining required data and information by mid-August.

The FDA said they will strive to complete their review expeditiously prior to the August 20 PDUFA date for pozelimab. However, if they are unable to complete their review before this date, the FDA said that they may need to extend their review by up to 3 months.

If they do extend the review, FDA has stated that they will continue to prioritize the review and complete it as early as possible.

Importantly, the FDA has also stated that their review of the Catalent manufacturing data in the context of the pozelimab BLA will support actions for both the pozelimab BLA and the aflibercept 8-milligram BLA resubmission, which has already been submitted. In summary, we and Catalent expect to submit by mid-August, all of the Catalent manufacturing data and information required to address the observations resulting from the pre-approval inspection.

The FDA has stated that they will strive to complete their review expeditiously prior to August 20. If not, we anticipate the FDA will act on pozelimab and aflibercept 8-milligram BLAs before the end of the third quarter.

In closing, we remain confident in our strategy of focusing investment on our internal R&D capabilities while exploring potential external collaborations as well as in our ability to deliver breakthroughs to patients and value to shareholders. With that, let me turn the call over to George.

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

Thank you, Len. I would like to start with our recent update on the aflibercept 8-milligram data in DME that Len referred to. At the Annual American Society of Retina Specialists Meeting, we presented the 2-year results from our PHOTON study. These data demonstrated that the vast majority of aflibercept 8-milligram patients randomized to the 12-week and 16-week dosing intervals continued to sustain vision and atomic improvements through 96 weeks. 89% of all aflibercept 8-milligram patients were able to maintain at least every 12-week dosing intervals for the entire 2-year period, while 84% of patients assigned to every 16-week dosing at baseline, were able to maintain that interval or extend beyond it.

On that point, many patients met the criteria for extension to longer intervals, with 44% meeting the criteria for greater than 20-week dosing intervals, including 27% who were eligible for 24-week dosing. The safety profile of aflibercept 8-milligram remained consistent with EYLEA. Sustaining vision and anatomic improvements while maintaining such extended dosing intervals over 2 years is unprecedented in the field.

Our results further strengthen the clinical profile of aflibercept 8-milligram and position this investigational medicine to become the future standard of care for retinal diseases. Later in the third quarter, we and Bayer our plan to share initial results from the second year analysis of the PULSAR study in patients with wet AMD.

Moving to our immunology and inflammation pipeline. On Dupixent, we look forward to the FDA decision for our sBLA in chronic spontaneous urticaria by October 22, 2023. In terms of DUPIXENT in patients with COPD, we and Sanofi are pleased to announce that DUPIXENT was granted breakthrough designation for uncontrolled COPD with an eosinophilic phenotype based on the positive results of the Phase III BOREAS study.

Based on ongoing discussions with the FDA, we expect that in addition to the BOREAS results, we will need to provide data from the Replicate Phase III NOTUS study to support a BLA and such data requirements remain under discussion with the FDA.

We continue to expect final results for the NOTUS study by mid-2024. Moving to itepekimab, our anti-IL-33 antibody, which is being evaluated for COPD in former smokers. In May, Sanofi announced that the Phase III AERIFY-1 and 2 studies had passed an interim futility analysis. These studies

remain on track for readout and regulatory submissions in 2025. Both itepekimab and DUPIXENT could transform the treatment paradigm for COPD by levering their distinct mechanism of action in reducing different types of inflammation that contribute to COPD.

Moving to oncology and combinations with Libtayo. In June, in an oral presentation at the ASCO conference, we presented data for the combination of fianlimab, our LAG3 antibody plus Libtayo which showed consistent response rates ranging from 56% to 63% across three independent cohorts of advanced melanoma patients including a new cohort of patients who had received prior anti-PD-1 therapy in the adjuvant melanoma setting.

These response rates represent about double the rate historically seen with anti-PD-1 monotherapy in similar settings, and clinically meaningful responses were observed in post-hoc analysis of various populations of interest including patients with poor prognosis factors and varying tumor PD-L1 expression levels.

The safety profile of fianlimab and the Libtayo combination in these cohorts appears to be generally consistent with the safety profile of the Libtayo monotherapy and other anti-PD-1 or PD-L1 agents, except for the higher rates of adrenal sufficiency, which were grade 2 or lower in the majority of cases, with all cases successfully managed with steroid replacement.

Our Fianlimab plus Libtayo Phase III studies in metastatic and adjuvant melanoma are enrolling patients as are the Phase II portions of the Phase II/III studies in advanced non-small cell lung cancer.

Next, on to bispecifics for solid tumors, which are being investigated in combination with Libtayo and other modalities. Later this year, we are planning to share initial clinical data for the combination of ubamatamab, our MUC16xCD3 bispecific plus Libtayo in advanced ovarian cancer.

Last year, we showed encouraging ubamatamab monotherapy data in advanced ovarian cancer, and we believe that combining it with Libtayo may lead to enhanced anti-tumor activity.

Moving to costimulatory bispecifics. We are currently exploring multiple different CD28 costimulatory bispecific antibodies in early clinical trials in a variety of tumor settings in combination with Libtayo, or with corresponding CD3 bispecifics.

In our Phase I study of REGN5678, our PSMA by CD28 costimulatory bispecific in advanced prostate cancer in combination with Libtayo which has demonstrated promising antitumor activity. The safety profile of this combination continues to pose a challenge, highlighted by a recently observed second grade 5 adverse event, or death. Although serious immune-mediated adverse events continue to be highly correlated to patients who experience profound responses, we have decided to discontinue enrollment of new patients with the full dose Libtayo combination, and explore PSMA by CD28 combination with lower doses of Libtayo.

We also will continue to explore PSMAxCD28 as a monotherapy where we are seeing antitumor activity in some patients, and we will explore PSMAxCD28 in combination with other immunotherapy modalities.

We believe our prostate cancer data support the exciting potential of costimulatory bispecifics, but with the challenge of focusing the response solely to the tumor. Our preclinical studies and mechanistic insights suggest a degree of immune-related adverse events seen when combining costims with PD-1 blockade may depend on the particular costim target and tumor type.

Moreover, combining costims with CD3 bispecifics may not result in these types of severe immune-mediated adverse events. Along these lines, our other costimulatory bispecific programs continue, including our MUC16xCD28 costim with Libtayo and our MUC16xCD28 costim with ubumatamab, both in ovarian cancer, as well as our EGFRxCD28 costim with Libtayo in colorectal and other cancers.

In these early dose escalation studies, we have observed limited immune-mediated toxicities to date. We're also excited about combining our costimulatory bispecifics with our CD3 bispecifics in our hem/onc programs, which continue to progress. We have initiated dosing of our CD22xCD28 costimulatory bispecific with our odronextamab CD20xCD3 bispecific in relapsed/refractory diffuse large B-cell lymphoma, which we hope can improve on the impressive efficacy demonstrated by odronextamab alone in that setting.

In terms of odronextamab monotherapy, U.S. and EU regulatory submissions for both relapsed or refractory follicular lymphoma and diffuse large B-cell lymphoma remain on track. Regarding linvoseltamab our BCMAxCD3 bispecific, we recently presented updated data at the ASCO annual meeting, demonstrating early, deep and durable responses in patients with heavily pretreated multiple myeloma with 71% objective response rate and 59% of patients achieving a very good partial response or better at the recommended 200-milligram dose with a median follow-up of only 6 months, with the data potentially improving as they mature.

We believe these data support linvoseltamab's best-in-class potential with differentiated efficacy, safety, hospital requirements and favorable dosing schedule. In the fourth quarter of this year, we are planning to present additional data with longer follow-up and to submit regulatory applications for linvoseltamab.

We also plan to start combination studies with a myeloma-specific costim next year.

Next, to genetic medicines. In the second quarter, we and Alnylam jointly announced the first human data suggesting that an siRNA can be used to silence pathological genes in the brain, which may open up an entirely new approach for fighting back against neurodegenerative and other central nervous system diseases.

We plan to initiate additional clinical programs for CNS diseases next year. As announced by our collaborators at Intellia, we plan to initiate the first *in vivo* CRISPR-based Phase III clinical program by year-end. Subject to regulatory feedback in patients with transthyretin amyloidosis cardiomyopathy.

And in terms of our targeted gene delivery pipeline, we hope to initiate our first clinical program in 2024 for hemophilia B.

In conclusion, Regeneron's R&D engine continues to grow and deliver differentiated late and early-stage opportunities, and we are looking forward to several important clinical milestones in the second half of this year.

With that, I will turn the call over to Marion.

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

Thank you, George. In the second quarter, Regeneron delivered impressive results across our commercial portfolio. Notably, Regeneron medicines currently lead multiple disease categories and our future is promising with short- and longer-term scientific innovations on the horizon.

As Len mentioned, we eagerly await the anticipated approval of aflibercept 8-milligram for retinal diseases. Beyond that, a robust late-stage pipeline supports additional commercial opportunities that we anticipate will continue to drive growth.

Starting with EYLEA, the anti-VEGF category leader in retinal diseases. U.S. EYLEA net sales were $1.5 billion, down 7% year-over-year and up 5% quarter-over-quarter. EYLEA total category share's remained stable at 46% over the last two quarters and at approximately 70% for branded share. At the end of the second quarter, there was minimal sequential change in wholesaler inventory levels compared to the levels at the end of the first quarter.

Our strategic focus is to maintain and grow Regeneron's anti-VEGF leadership, and we're well positioned to deliver on this goal in an increasingly competitive category. Last week at ASRS, we presented our 2-year data in diabetic macular edema, which further confirmed the unprecedented durability of aflibercept 8 milligram, with 44% of patients assigned intervals of at least 20 weeks at the end of their second year.

Market enthusiasm remains high for this important innovation and our commercial team is ready and excited to launch aflibercept 8-milligram upon approval.

Moving now to Libtayo. Global net sales were $210 million, up 49% year-over-year on a constant currency basis. In the U.S., net sales were $130 million, up 43% and driven by steady growth in non-melanoma skin cancer and strong growth in lung cancer. In lung cancer Libtayo use in new

patient share is accelerating both monotherapy and in combination with chemotherapy. With an expanding base of prescribers in the community and academic settings. Outside the U.S., Libtayo net sales were $80 million, a 58% increase on a constant currency basis. Growth was driven by demand in the non-melanoma skin cancer indications and initial launches in lung cancer.

We expect to drive accelerated performance as we build Regeneron's presence in key international markets and secure access and reimbursement for lung cancer indications. And lastly, to DUPIXENT, which continues to revolutionize the lives of patients with type 2 diseases. Global net sales were approximately $2.8 billion, up 34% year-over-year on a constant currency basis and up 12% compared to the first quarter of 2023.

In the U.S., net sales grew 33% year-over-year to $2.1 billion, driven by growth across all indications and age groups. Once again, DUPIXENT is the #1 prescribed biologic medicine for new-to-brand patients across all approved indications and is the category leader in total prescriptions in 4 out of 5 indications. We see impressive uptake across our recent U.S. launches with significant opportunity for future growth.

In eosinophilic esophagitis, well over 15,000 patients have been initiated since launch, and we are actively investing in disease awareness initiatives to empower patients to seek diagnosis and treatment for this debilitating disease. Our pruigo nodularis launch is off to a fast start with physicians rapidly recognizing DUPIXENT as the go-to treatment for this often-underdiagnosed dermatologic condition.

Additionally, we look forward to our October 22 PDUFA date. In chronic spontaneous urticaria, where we estimate DUPIXENT could benefit up to 300,000 U.S. patients. We also continue to generate impressive growth across atopic dermatitis, asthma and nasal polyps, DUPIXENT's three largest indications.

There is robust demand among all indicated age groups with a significant opportunity for future growth beyond the hundreds of thousands of patients around the world whose lives have already been transformed by DUPIXENT.

In summary, we delivered a strong commercial performance in the second quarter with Regeneron's Medicines position for sustained growth. We continue to demonstrate industry-leading execution across our current portfolio, and we are prepared to maximize opportunities from our robust pipeline with the goal of extending Regeneron's scientific innovations to even more patients. Now I will turn the call over to Bob.

Robert E. Landry - Regeneron Pharmaceuticals, Inc. - Executive VP of Finance & CFO

Thank you, Marion. My comments today on Regeneron's financial results and outlook will be on a non-GAAP basis unless otherwise noted. Regeneron's second quarter results demonstrate continued growth and strong financial performance across the organization.

Second quarter 2023 total revenues increased 11% year-over-year to $3.2 billion, driven by strong DUPIXENT sales growth, coupled with improving profitability within our Sanofi collaboration and continued momentum from Libtayo.

Second quarter diluted net income per share was $10.24 on net income of $1.2 billion. Moving to collaboration revenue and starting with Bayer. Second quarter 2023 ex U.S. EYLEA net product sales were $886 million, up 4% on a constant currency basis versus second quarter 2022. Total Bayer collaboration revenue was $377 million, of which $350 million related to our share of EYLEA net profits outside the U.S.

Total Sanofi collaboration revenue was $944 million in the second quarter and grew 39% versus the prior year. Our share of profits from the commercialization of DUPIXENT and KEVZARA was $751 million, an increase of 51% from the second quarter of 2022, reflecting higher volumes and an improving margin profile for DUPIXENT.

We expect further margin expansion from the collaboration driven by continued DUPIXENT global sales growth, coupled with higher gross margins due to significant drug substance yield improvements resulting from dupilumab manufacturing process enhancements. These factors are also contributing to a gradual increase in the rate in which we are repaying the antibody development balance to Sanofi.

Once this balance is fully repaid in the next few years, we expect a meaningful step-up in our share of Sanofi collaboration profits. Recall that a portion of our Sanofi collaboration revenue is related to the manufacturing of commercial supplies for which we are reimbursed by Sanofi. As we

continue to phase in the higher yield manufacturing process for DUPIXENT, we expect these second half reimbursements to be approximately 25% lower than the first half of 2023, with the fourth quarter expected to be the lowest of the year.

Other Revenues were $69 million in the second quarter, up 17% versus the prior year. We continue to expect other revenue to be higher in the second half of 2023 as compared to the first half. Recall that other revenue primarily includes reimbursements for the manufacturing of certain Regeneron discovered products commercialized by other companies, including ex-U.S. PRALUENT ARCALYST and ZALTRAP as well as royalties for Ilaris and our share of global profits for ARCALYST.

Moving now to our operating expenses. Second quarter 2023. R&D expense was $974 million, representing continued investment in our robust pipeline. Year-over-year R&D growth was primarily driven by higher head count and related costs and funding of the company's pipeline, which encompasses approximately 20 late-stage or potentially registrational studies, including our ongoing aflipercept-8 mg studies, Phase III studies in earlier lines of therapy for our hem/onc product candidates and our advancing fianlimab development program.

The increase in R&D expense was also driven in part by the impact of the 2022 amendments to the Sanofi collaboration agreement and increased manufacturing activity associated with the company's earlier stage product candidates. SG&A was $562 million in the second quarter, reflecting the ongoing build-out of our ex U.S. operations following the acquisition of global rights to Libtayo last year, higher head count and related costs and higher contributions to an independent not-for-profit patient assistance organization.

Second quarter 2023 COCM was $213 million, up 44% versus the prior year. driven by manufacturing costs associated with higher DUPIXENT volumes. As we progress the phase-in of the improved manufacturing process for DUPIXENT, we expect COCM in the second half of this year to decline versus the first half as our unchanged 2023 COCM guidance reflects, with the fourth quarter expected to be the lowest of the year.

Now to cash flow and the balance sheet. In the first half of 2023, Regeneron generated approximately $2.1 billion in free cash flow we ended the second quarter with cash and marketable securities less debt of approximately $12.6 billion. We continued to opportunistically deploy cash towards share repurchases throughout the second quarter buying back $723 million of our shares. At current levels, we remain buyers of our shares.

And as of June 30, approximately $2.3 billion remained available for repurchases under our existing authorization.

Finally, we've made some minor changes to our full year 2023 guidance ranges based on our first half results and our latest outlook for the remainder of the year, we have tightened guidance ranges for 2023 SG&A and R&D spend and provided updated guidance ranges for our effective tax rate.

A complete summary of our latest full year guidance is available in our press release issued earlier this morning.

In conclusion, Regeneron delivered positive financial results in the second quarter of 2023 and we remain excited for the potential upcoming launch of aflibercept 8 mg in the third quarter. With that, I will now pass the call back to Ryan.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - VP of IR

Thank you, Bob. 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 only be able to 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) Our first question comes from the line of Evan Seigerman with BMO.

Evan David Seigerman - BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst

So on the 8-milligram CRL, do you have any idea if it's a Class I or Class II resubmission? And you say that FDA is going to take action in the third quarter or could take action. What does that mean? Are they going to provide an approval decision? Or is that just going to be acceptance of a refiling.

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

Evan, it's Len. Thanks for your question. So just to clarify, the FDA has not classified the resubmission as Class I or Class II because they have said that the time line for pozelimab will be governing what happens with our 8 milligrams. So let me remind you what happened. There was a pre-approval inspection for both products. The pozelimab is for our ultra-rare disease CHAPLE disease, and it has a PDUFA date of the 20th.

What the FDA has said is that they will review the remediation efforts in the context of the pozelimab BLA. And therefore, whatever happens there will govern the time line and results. And when we say we expect them to take action, we mean that we expect them to make an approval or not decision.

If they find the manufacturing remediation acceptable for the pozelimab, then we think they'll be in a position to promptly make a decision on approval for the 8 milligrams. Does that answer your question?

Operator

Our next question comes from the line of Tyler Van Buren with TD Cowen.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

So the time line to the FDA potentially taking action by the end of this quarter on high dose EYLEA is very encouraging. Investors are clearly surprised by the short line. So kudos to you all for executing, but as we think about the data submission in a couple of weeks, what additional details can you provide regarding the manufacturing data and other information that are required from Catalent and how feasible it is to review this in a few days prior to the pozelimab decision date on August 20.

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

Right. Great question. So we've been in very close contact with Catalent and the FDA with multiple meetings, oral, written and so forth. And we have a clear understanding of what's required from an information point of view and from a data point of view.

The submissions have been on a rolling basis that as Catalent has completed work, they've submitted data and information already to the FDA. There is very little that will be left for the last submission at the middle of August.

And that's why the FDA has told us and they know what's coming, that they will strive to expeditiously review that. If they can't get that done by the few days before the pozelimab PDUFA date, they have told us that they will prioritize our review and do that as soon as possible.

That's why we have confidence about this getting done in this quarter.

So to summarize, the data has been coming in on a rolling basis. We have everything we need, the last piece of information will be rolling in and submitted by the middle of the month. the FDA will strive expeditiously to review that return in time for the August 20 PDUFA date.

But if not, there'll be a clock extension for up to 3 months, but they have told us that they will prioritize our review. And that's why we believe it will get done, if not in time for the pozelimab PDUFA date, in the near future thereafter.

Operator

Our next question comes from the line of Mohit Bansal with Wells Fargo.

Mohit Bansal - Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst

And really thank you very much for providing all the clarity on the filing situation right now. Maybe taking -- so just trying to understand this a little bit more. So is it fair to say you have already submitted everything for pozelimab. And the remaining part is related to high-dose EYLEA only? Is that fair?

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

Actually, the way you should think about it, we've submitted everything we need for pozelimab except for the final remediation of the preapproval inspection, which applies both to pozelimab and to the 8-milligram EYLEA. So it's a single preapproval inspection, same data and information required for both. Once that is in, then we will have completed everything necessary for pozelimab and for the EYLEA 8 milligrams. They are linked together. The FDA has clearly stated to us that the review of this remediation in the context of the pozelimab BLA will govern what happens to the 8-milligram remediation.

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

And I think it's fair to say there's nothing specific to either pozelimab or aflibercept about the data. This has to do, as Len said, with general manufacturing processes and operations at the Catalent manufacturing facility, particularly with this one manufacturing line.

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

Yes. That's a very good point, George. So that's why the single preapproval inspection applies to both products. It wasn't the product specifically, it was the processes and validation on the line that fills the two products. So one remediation satisfies both, all the data and information that are being submitted on a rolling basis. The last piece comes in, in the middle of August, the FDA is aware of this.

They've told us in writing that they will strive to review that expeditiously. If they get it done before the end of the PDUFA, the original PDUFA clock, that's great. If they don't, they'll consider it an amendment that will set the clock back 3 months. But notwithstanding that 3 months, they've told us that they will continue to prioritize our review. So we're very pleased, and we're working very hard. Catalent is working very hard. The FDA is working very hard. Everybody wants this done properly and finished and properly remediated.

Operator

Our next question comes from the line of Tim Anderson with Wolfe Research.

Timothy Minton Anderson - Wolfe Research, LLC - MD of Equity Research

I have a question on Vabysmo. So Roche at Q3 said they're capturing 30% of treatment-naive patients, which seems like a quite high figure, frankly. And then they said afterwards that it's not the extended dosing that's driving this as much as it is the better drying that they say docs are seeing with their product. I'm wondering how those comments kind of line up to what you're seeing play out in the U.S. market?

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

Sure. So Tim, I will comment on our EYLEA performance. And as I just shared with you, the performance in the quarter was strong. Certainly, we see EYLEA steadily as the standard of care in the anti-VEGF category.

We continue to capture not only naive patients but also another big source of business is switch patients from Avastin.

Obviously, the other branded competitors are smaller in market today. But I would say that beyond your comment, probably best to get more clarification from the individuals who are commercializing faricimab in the market. But certainly, I do want you to know that we are seeing continued strength in EYLEA performance.

And obviously, very much look forward to having the potentially game-changing opportunity bringing aflibercept 8-milligram into the marketplace where the profile of efficacy, safety and durability has so many KOLs and prescribers excited based on what they've seen recently in the clinical data presented at ASRS.

Operator

Our next question comes from the line of Chris Raymond with Piper Sandler.

Christopher Joseph Raymond - Piper Sandler & Co., Research Division - MD & Senior Research Analyst

Just maybe another market VEGF market-related question. So I know these extended dose therapies have benefits in and of themselves on the face of them, but there's been some decent level of market chatter around docs looking to free up injection capacity. Specifically to make room for geographic atrophy patients and specifically with the Apellis drug.

Just maybe curious how widespread was that notion before the Syfovre safety issue. And now with the issue, have you noticed a discernible shift among docs who were talking about that. And then maybe a related question. You guys have talked, I think, about an early effort of your own in geographic atrophy. Clearly, the market is sizable. When could we expect to hear more about that effort?

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

So let me share first in terms of the market dynamic. I think the most exciting thing and most important thing about a aflibercept 8-milligram is that it gives prescribers for all of their patients, whether a naive patient, a patient currently on EYLEA or a patient on another anti-VEGF category product the opportunity to decide if that patient is a candidate when we launch and when we have an FDA approval, if the patient is a candidate for aflibercept 8-milligram that does have benefit to the patient and prescriber and potentially to the office capacity and patient flow.

I think it's premature to comment on a category that we're not directly involved in. We are, though, very focused on making sure that we are ready for launch and certainly at the proper time, educating all stakeholders on the aflibercept 8-milligram once we have an approval.

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

And in terms of our own efforts, as I'm sure many of you are aware, we've been very active with what we feel are very innovative approaches in the complement blockade field. And we believe that we may have an approach that may allow potentially treatment in these retinal diseases. While avoiding some of the very concerning adverse events having to do with issues like occlusive vasculitis and so forth, and you'll be hearing much more about those efforts in the short term.

Operator

Our next question comes from the line of Carter Gould with Barclays.

Carter Lewis Gould - Barclays Bank PLC, Research Division - Senior Analyst

Thanks for all the transparency. Maybe switching gears a bit in terms of the update on your costim and the report of the death and the and the change in the dosing paradigm with 5678 in combination with Libtayo. George, maybe you can speak about the implications for other combination efforts of CD28 with Libtayo. Is this going to require a lower dosing with those efforts with the Libtayo portion? And just the broader implications there and just still your level of confidence that you can kind of thread that needle in terms of the dosing levels.

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

Right. No, great question. Obviously, as you know, in cancer, the biggest hurdle is actually coming up with approaches and new classes of agents that have the ability to really change the efficacy paradigm to really bring new ability to address cancers that have previously been untreatable or refractory to treatment.

So I think that, that excitement continues with the costim platform in terms of all of the science and the preclinical modeling and predictions have really delivered in terms of showing that this new class does seemingly have the ability to really change the efficacy paradigm.

But now we have to balance that, as you said, with the safety because with more efficacy, which is often seen in the cancer field comes more safety Concerns. To what you just said, what we've seen preclinically, and we're now beginning to see it in the clinic, that the amount of associated immune adverse events is related to the particular costim target.

So what you see for one costim in doesn't necessarily apply to the other costim. So we are, as you said, for our PSMA costim, moving now to lower doses of the Libtayo because the full dose combination while it seems like it has the potential to be very efficacious also has, in some cases, these associated only -- remember, only in the patients who are having deep responses, these associated in some cases, that can be very serious, even resulting in death associated in new adverse events.

So -- we're moving away from full dose combinations there, and we're going and hoping that we can maintain some level of the efficacy, but avoiding these very serious immune-related adverse events. We're not doing that yet because we're not seeing these sort of immune-related adverse events with our other costims. And the other very, very important thing, just to remind you from our preclinical modeling, these types of immune-related adverse events that we're seeing with the PSMA in combination -- costim in combination with Libtayo, are not seen preclinically when you combine with the CD3 bispecific.

And so we are very aggressively trying to move forward those programs as well, where we hope we may even have a better efficacy safety profile. So it's both a very exciting time to have these very active molecules.

Remember, I remind you, we have three classes now, three independent classes of very active molecules that have been individually validated in our portfolio. We have the checkpoint inhibitors, in particular, our PD-1 and our LAG-3 checkpoint inhibitors, which are validated. We have our CD3 bispecifics which are validated, and we now have our costims, which are validated from the efficacy perspective. Very exciting time to be mixing and matching them. The challenge is to mix and match them appropriately to maximize the signal to noise, the therapeutic benefit relative to the potential adverse events we would see in the patients.

Operator

Our next question comes from the line of Salveen Richter with Goldman Sachs.

Salveen Jaswal Richter - Goldman Sachs Group, Inc., Research Division - VP

And nice updates this morning. Clearly, the possibility of a permanent J code now has moved to April, and it shortens the runway for patients switching from EYLEA ahead of potentially loss of exclusivity in May. So kind of a 2-part question here. What are the dynamics around this? And how do you, on one hand, kind of maintain and grow the switch population from EYLEA. But secondly, how should we think about the uptake of high-dose EYLEA without a permanent J code?

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

Hi Salveen. I'll get started. Certainly, we're conscious of the dates and the requirement for submissions to CMS that occur at the start of a quarter. We would estimate potentially the time frame that you're referencing, if we have an approval in the third quarter. What I would share is that we anticipate use of aflibercept 8-milligram after approval and launch before we have the permanent J code. Retina specialists are sophisticated in their reimbursement capabilities at the office level. They are experienced with newer products coming into the marketplace on a fairly regular basis, and how to make certain that they validate reimbursement for products prior to having the permanent J code under a temporary J code.

So obviously, we want to have the permanent J code that will be a positive. But certainly, we do see the opportunity for uptake across patient types prior to that situation with CMS.

Operator

Our next question comes from the line of Terence Flynn with Morgan Stanley.

Terence C. Flynn - Morgan Stanley, Research Division - Equity Analyst

Len, I know we've talked about this before, but the company has been somewhat nontraditional on pricing decisions historically. You guys priced EYLEA at a discount to Lucentis. You worked with ICER on DUPIXENT pricing. So just wondering why we shouldn't expect it similar approach here with high-dose EYLEA.

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

Thanks, Terence. If your comments referencing similar mean thoughtful and appropriate, we would agree.

Operator

Our next question comes from the line of Brian Abrahams with RBC Capital Markets.

Brian Corey Abrahams - RBC Capital Markets, Research Division - Senior Biotechnology Analyst

Congrats on all the progress and appreciate all the details. Maybe just another clarification on 8-milligram aflibercept. Can you characterize your level of confidence that a reinspection would not be required? Have you had any interactions or feedback with the agency around this? And is there a defined period of time where the FDA would need to wait reinspection or not to ensure that the remediations are sustainable before approving the BLAs?

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

Great. Thanks for your question. Well, we've tried to be 1,000% transparent as usual at Regeneron. And this is really let me just see if I can summarize it again, what we know. We've been in close contact with the FDA as has Catalent. We know what the remediations required are, and we've been submitting them on a rolling basis.

We expect to submit the last requirement by the middle of August, and that will be several days before the PDUFA date for the pozelimab BLA. The FDA has been very clear that they will strive to expeditiously review that. If they can, great. If they can't, they said there would be a 3-month clock extension. But even with the 3-month clock extension, they've been very categorical in saying that they would prioritize their review and try and get it done as soon as possible.

Those facts are what led us to believe it would be done during the third quarter. In all of this is the fact that there has been no need, no discussion, no indication whatsoever that a reinspection would be necessary.

The FDA, of course, is free to make those decisions but we have not seen any indication of that in our very detailed and close contact. So we've given you our best estimate at this point.

Operator

Our next question comes from the line of Chris Schott with JPMorgan.

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

Can I just come back to the CD28 PSMA update. Maybe just elaborate a little bit more in terms of the approach of lowering the PD-1 exposure to address the safety issues here and taking that approach versus trying to work to further adjust the dosing of the bispecific piece of the equation?

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

Well, we should say that we are adjusting both doses. We have been already exploring a variety of doses from very low doses to the highest active doses on the costim side, but we've been doing all of them in the context of the full dose of Libtayo.

So now what we're doing is we're exploring some of the doses that are active particularly ones that are active as monotherapy, as I mentioned, there is monotherapy activity with the PSMA costim and now we're, to try to decrease these immune-related adverse events.

Let me remind you, they are in the same sort of class of immune-related adverse events that you do see with checkpoint inhibitors in general. We're just seeing them in some patients, the one with the biggest responses, in some cases to a greater extent.

So we're hoping that lowering the checkpoint inhibition may allow us to adjust the therapeutic window there. But we are, as you're saying, dealing with a couple of different doses of the costim, but now we're incorporating lower doses of the Libtayo into the program as well.

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

I think what George said earlier, and just maybe bears repeating is that he said that we're starting with the good position of having very impressive efficacy, one and two, side effects that are for the most part in the patients who are benefiting with the efficacy. That's a very good position to begin to explore and how to get the therapeutic index or signal to noise, as George called it right.

Operator

Our next question comes from the line of Dane Leone with Raymond James.

Dane Vincent Leone - Raymond James & Associates, Inc., Research Division - MD & Biotechnology Analyst

Congratulations on the updates and best of luck with the resolution of the reviews for pozelimab and 8 mg aflibercept. I actually want to ask you to expand a bit on your discussions with the FDA and potential filing or early filing on DUPIXENT for COPD. The point I'd like a little bit more clarity on is specifically what you may be able to have from NOTUS before the final readout of that study that you could potentially include in a package with the BOREAS results to get the FDA comfortable with an accelerated review for that indication?

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

Yes. What we know right now is that we're going to need data from NOTUS. And right now, as we said, we are still in discussions on what that data could be. And so right now, we don't have any details to give you.

Operator

Our next question comes from the line of Colin Bristow with UBS.

Colin Nigel Bristow - UBS Investment Bank, Research Division - Analyst

Congrats on the quarter and on the progress. Just maybe one on the itepekimab interim. Can you share anything on the futility thresholds? And if not specifically, then could you say how it sort of fared relative to BOREAS?

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

I don't think we have anything specific. This was handled by the Data Safety Monitoring Committee, sort of a standard approach. We're pleased that we passed it. And we will look forward to further data at the end of the study.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. – VP of IR

Yes. And both we and Sanofi are blinded to that. We only got the go decision from the independent data monitoring committee. So we'll proceed to a final readout for both of those studies.

Operator

Our next question comes from the line of Brian Skorney with Baird.

Luke P. Hermann Robert W. Baird & Co. Incorporated, Research Division – Research Analyst

This is Luke on for Brian. Can you just provide a little bit more color on what drove the Libtayo growth this quarter? Was there any stocking? Or was it largely demand-based?

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

Luke, and I'm pleased to share it is demand growth. Certainly, we see continued and steady performance across our skin indications, both cutaneous squamous cell carcinoma and basal cell carcinoma -- in addition to that, it is exciting that we are seeing not only an increase in the number of prescribers for our lung cancer indications, but the depth of prescribing is improving and increasing in both the community and also academic settings. That is demand based, it is not stocking based.

Operator

Our next question comes from the line of David Risinger with Leerink Partners.

David Reed Risinger - Leerink Partners LLC, Research Division - Senior MD

So my question is for George on the costims, please. You mentioned that you haven't seen the immune AE's with respect to your other Costim trials. Could you please comment on whether the dosing step-ups at this point are close to the higher dosing levels that you're stepping back from in the PSMA trial. I'm just trying to contextualize whether you really have advanced those other trials to the point to really know whether you're going to have similar problems in your other Costim trials?

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

That's a very good and fair question. And those programs are at earlier stages. So we won't know until we're more advanced, whether when we get to the same sort of efficacy type levels, do we have the same sort of immune-related adverse event associations or not? What I was referring to is in the preclinical studies, the amount of this associated T cell activation that can lead to these sorts of immune-related adverse events varies depending on the tumor class and on the costim itself.

So based on that, we would expect to see different ratios of immune-related adverse events. Those other programs, though right now are all in stages where they were in a full dose Libtayo combinations at this point.

Operator

Our last question is from Akash Tewari with Jefferies.

Akash Tewari - Jefferies LLC, Research Division - Equity Analyst

I'll switch it up. I guess maybe for your obesity program, you had data at the ADA showing synergy with your myostatin inhibition program when combined with the GLP-1. I guess the natural observation here is Regeneron doesn't currently have a program in development. Is there any interest in acquiring one externally via BD or partnership at this time?

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

Well, what we would say is we do think that, obviously, there's a lot of focus on obesity and particularly these new agents that are causing a large amount of weight loss. But as you described as being increasingly recognized that the quality of this weight loss may prove challenging that many patients are actually losing muscle or lean body mass which is -- can be very detrimental, particularly if they stay on these therapies or yoyo on and off them.

That can really lead to substantial changes over time and body composition and can be very debilitating for patients. And as you said, we've had a long investment in programs that can maintain muscle mass in various settings and we've shown that they can maintain or even grow muscle mass in the setting of these types of obesity treatments in our preclinical modeling.

So obviously, it is a very exciting opportunity to think about, which is can we combine some of our muscle preservation or growth strategies and biologics to prevent these concerning side effects that are being seen with the new class of profound weight loss agents.

And so we are very actively pursuing everything that we can imagine and hopefully, we'll be providing updates on our approaches as time goes along.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. – VP of IR

All right. Thanks, George, and thanks for everyone who dialed in today and for your interest in Regeneron. We apologize to those remaining in the queue that we did not have a chance to hear from. As always, the Investor Relations team is available to answer any remaining questions. Thank you once again, and have a great day.

Operator

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