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REGN.OQ - Q1 2024 Regeneron Pharmaceuticals Inc Earnings Call

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Welcome to the Regeneron Pharmaceuticals First Quarter 2024 Earnings Conference Call. My name is Josh, 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. - SVP of IR & Strategic Analysis

Thanks, Josh. Good morning, good afternoon and good evening to everyone listening around the world. Thank you for your interest in Regeneron and welcome to our first quarter 2024 earnings conference call. An archived 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 March 31, 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 IR 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 S. Schleifer - Regeneron Pharmaceuticals, Inc. - Co-Founder, President, CEO & Co-Chairman

Thanks, Ryan. Thanks to everyone joining today's call. Regeneron is off to a strong start in 2024, reflected in our solid first quarter financial results as well as the progress we have made across our pipeline in the first 4 months of the year. For my remarks today, I'd like to briefly review some of our key performance drivers and then discuss a few of our more differentiated development programs, which have the potential to drive sustainable long-term growth for the company and value for our shareholders. After my remarks, George will provide an update on our pipeline. Marion will then review our commercial performance, and Chris will discuss our financial results. First quarter 2024 revenues grew 7% after excluding last year's revenue contribution from our COVID antibodies. Growth was primarily driven by Sanofi collaboration revenues and Libtayo global net product sales, which grew by 14% and 45%, respectively.

Dupixent global net product sales were $3.1 billion, up 24% reflecting strong growth across all approved indications. EYLEA HD generated $200 million in its second full quarter on the U.S. market outperforming recent launches in the anti-VEGF category. Now with the permanent J-Code in place, improving payer coverage, broad prescriber familiarity and satisfaction with the EYLEA HD clinical profile and direct-to-consumer TV promotion underway. We continue to position EYLEA HD as the new standard of care for retinal diseases.

Shifting to chronic obstructive pulmonary disease or COPD where Regeneron and Sanofi have 2 differentiated opportunities to transform the treatment paradigm for patients living with this debilitating disease. As announced in February, our sBLA for Dupixent for the treatment of COPD with type 2 inflammation was accepted by the FDA for priority review with a June 27 PDUFA date.

During its review of our submission, the FDA has requested additional efficacy analyses, including an information request received earlier this week regarding subpopulations from the BOREAS and NOTUS pivotal studies. Our analyses across these requested patient subgroups indicate a consistent and clinically meaningful reduction in COPD exacerbations. While the FDA has requested these analyses to be submitted by the end of May, we anticipate providing them substantially sooner. We and Sanofi are confident that these additional analyses strongly support the approval of Dupixent and eosinophilic COPD. If the FDA determines that they need additional time to review these analyses, a decision on the sBLA could be delayed for up to 3 months.

We and our partner, Sanofi, are preparing for launch that many pulmonologists, respiratory key opinion leaders and their patients are eagerly anticipating. If approved Dupixent will be the only biologic therapy for COPD and the first new treatment approach for this disease in more than a decade. There is a high unmet need in COPD with type 2 inflammation with approximately 300,000 eligible patients in the United States and another approximately 300,000 eligible patients in the EU and Japan, where we are also seeking regulatory approvals. Turning to itepekimab our IL-33 antibody, which is being evaluated in former smokers with COPD regardless of eosinophil phenotype. We remain on track to report results and enable potential global regulatory filings in the second half of next year.

Itepekimab can potentially address up to 1 million patients in the G7 countries, while China also represents a significant opportunity. We are very excited about potentially bringing these important new therapies with COPD patients while expanding our commercial respiratory franchise. In a moment, George will describe another key opportunity in our pipeline involving Dupixent in combination with our BCMAxCD3 bispecific antibody

linvoseltamab which we believe has the potential to address any severe allergy and allow the millions of severe allergy sufferers to stop living in fear of an accidental exposure. Moving from linvoseltamab in severe allergy to its differentiated opportunity in multiple myeloma where it is currently under FDA and EMA review in the relapsed refractory setting. In our registration-enabling data set, while cross trial comparisons caveat supply, we believe linvoseltamab represents a best-in-class opportunity because it has the highest objective response rates and complete response rates at similar follow-ups observed across the BCMA bispecific class to date requires the least number of days in the hospital compared to other drugs in the category and is the only BCMAxCD3 agent currently under review or are already approved by the FDA that evaluated every 4-week dosing.

If approved, we believe these are all important considerations for patients, caregivers, providers and payers that could drive linvoseltamab adoption. In closing, I'm excited and energized by the differentiated opportunities in our pipeline, which now has over 35 programs in clinical development spanning many distinct therapeutic areas. Our commercial team continues to execute well and is building momentum in competitive categories, and we continue to deploy capital with the goal of driving shareholder returns over time. With that, I'll turn the call over to George.

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

Thanks, Len. Since Len covered the status of the Dupixent and itepekimab programs in COPD in great detail, I'd like to start with a bit more about our innovative treatment approach for severe allergies, a first-ever combination of an immunomodulatory antibody that is DUPIXENT with a bispecific antibody. Despite the remarkable benefit demonstrated by DUPIXENT across multiple diseases characterized by allergic or type 2 inflammation, DUPIXENT alone does not immediately reverse severe allergies by itself. These allergies are caused by high levels of an immunoglobulin class known as IgE made by long-lived plasma cells. This has caused some to refer the E in IgE as E for evil. Although DUPIXENT will prevent formation of new IgE plasma cells, it does not eliminate those that have already formed.

Regeneron scientists have shown that these allergy causing IgE plasma cells can be rapidly eliminated with a short course of treatment with our bispecific antibody known as linvoseltamab. While Dupixent treatment will then prevent these cells from returning as recently highlighted in our publication in Science Translational Medicine. We have commenced our proof-of-concept clinical trial to explore the potential for this combination approach to eliminate severe food allergy. We are hoping to see initial observations from this small study later this year, which will inform next steps.

Moving on to oncology and libtayo combinations. Early clinical results of our LAG-3 antibody fianlimab in combination with libtayo suggest that these antibodies represent one of the most promising checkpoint inhibitor combinations in clinical development. Recall, fianlimab libtayo demonstrated potential for best-in-class efficacy in first-line metastatic melanoma with objective response rates of approximately 60% across 3 independent cohorts from our first-in-human study with a safety profile that is similar to that seen with anti-PD-1 monotherapy. With longer-term follow-up, these initial responses continue to deepen, including patients converting into complete responses. We look forward to presenting updated results from these expansion cohorts in the second half of this year.

Encouraged by these initial results, last year, we initiated a Phase II/III study of the combination of fianlimab and libtayo in first-line metastatic melanoma. This study is enrolling faster than expected and will now be conducted solely as a Phase III study with the final analysis to be reported during 2025. These pivotal melanoma data will inform whether fianlimab and libtayo have the potential to emerge as a new standard of care in melanoma.

Next, to our bispecifics for hematology oncology. Regarding odronextamab, our CD20xCD3 bispecific, as announced in March, we received complete response letters from the FDA for our BLA for relapsed/refractory follicular lymphoma and relapsed/refractory diffuse large B-cell lymphoma. The only approvability issue was related to the limited enrollment of these confirmatory trials, which we intend to address as we continue to enroll patients in these studies. The EU decision on odronextamab application is expected in the second half of this year.

Moving on to linvoseltamab. As Len noted, this bispecific continues to demonstrate a potentially best-in-class profile in late-line myeloma in terms of efficacy, safety, dosing and hospitalization burden. In an oral presentation at the recent AACR medical meeting, we presented results of an 11-month median follow-up of 117 patients. A 71% objective response rate with 46% of patients achieving a complete response or better. We are planning to present updated 14-month follow-up results at the upcoming EHA meeting in which we anticipate observing a further deepening of

responses. Regarding the ongoing FDA review, we believe the confirmatory study will be sufficiently enrolled to support approval. We're also evaluating linvoseltamab in earlier stages of myeloma and in precursor conditions such as smoldering myeloma and monoclonal gammopathy of unknown significance or MGUS.

Next, to bispecifics for solid tumors. Our cost inventory bispecific antibodies are being tested in numerous studies, including as monotherapies as well as in combination with CD3 bispecifics and with libtayo. Our EGFRxCD28 bispecific in combination with libtayo, we are planning to present updated dose escalation results in an oral presentation at ASCO, most notably, in microsatellite stable colorectal cancer, a tumor historically unresponsive to immunotherapy, EGFR by CD28 in combination with libtayo demonstrated antitumor activity.

Regarding safety, to date, we have not observed severe immune-related adverse events with this agent at our recommended Phase II dose. Based on these data, we are enrolling dose expansion cohorts testing our EGFRxCD28 costim bispecific plus libtayo in various cancers, 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 PSMA by CD28 costimulatory bispecific, which is already demonstrating promising activity in prostate cancer in combination with libtayo. We will soon initiate combination treatment of our PSMAxCD28 costim bispecific with our PSMAxCD3 bispecific, which based on preclinical studies, may maintain efficacy but with better tolerability.

We're also evaluating our MUC16xCD28 costimulatory bispecific with ubamatamab, or MUC16xCD3 bispecific as well as with libtayo, our CD38xCD28 costim with linvoseltamab for myeloma and our CD22xCD28 costim with odronextamab for lymphoma. Moving on to our classical hematology pipeline. Our C5 approach involves a first-in-class combination of an sRNA with an antibody for a more complete target blockade in our initial clinical data supports potential best-in-class efficacy in paroxysmal nocturnal hemoglobinuria or PNH.

Results from the preliminary cohort of the PNH Phase III study will be presented at the EHA conference in June with additional results expected later this year. In addition to PNH and myasthenia gravis, which are already enrolling their respective pivotal trials, we are planning on extending the systemic combination approach to geographic atrophy in dry AMD with the first pivotal study in GA expected to get underway this year.

We are also anticipating proof-of-concept data later this year for our 2 complementary Factor XI antibodies in the setting of prevention of venous thromboembolism after knee replacement surgery. Depending on these data, 1 or both of these antibodies could remain on a rapid path to registrational studies, which could begin by late 2024 or early 2025. We -- our first-in-class antibody TMPRSS6, a genetically validated target for iron overload diseases such as beta thalassemia, is also making progress. This antibody has potential to meaningfully reduce toxic organ iron in patients whom iron chelation is inadequate or intolerable.

Updated proof of mechanism data in healthy volunteers will be presented at the upcoming EHA conference. These results demonstrated deep sustained reductions in serum iron and robust induction of the liver hormone hepcidin, supporting the potential to release iron from organs. We are on track to start a Phase II proof-of-concept study in beta-thalassemia patients in the second half of the year.

Moving to obesity. Our most advanced approach is designed to address potential negative consequences of widespread use of GLP GIP receptor agonist. As it 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 antibodies to myostatin-related pathways may prevent this muscle loss. Indeed, our data in obese nonhuman primates show that combining semaglutide with trevogrumab, our antibody targeting myostatin with or without garetosmab, our antibody targeting Activin A, or myostatin 2, demonstrated a comparable reduction in body weight at week 20 relative to semaglutide monotherapy, but with improved quality of weight loss resulting in more fat loss while preserving or even increasing lean mass.

Part A of our proof-of-concept study in healthy volunteers intended to demonstrate safety of a higher dose of trevogrumab, has completed enrollment. Note that over 400 subjects, including healthy volunteers in sarcopenic patients have been dosed with trevogrumab throughout its clinical development with no meaningful safety or tolerability concerns observed to date. Part B of the study, which will evaluate muscle preservation antibodies in combination with semaglutide in obese participants remains on track to start enrolling mid-year assuming a reasonable pace of

enrollment, we expect to report top line results, including changes in body weight, fat mass and muscle mass in second half of 2025. I will conclude with our genetic medicines effort.

At the upcoming ASGCT conference, we will present updated data from our DB-OTO gene therapy program for genetic hearing loss. The first patient treated with this therapy, a 10-month old girl who is profoundly deaf at baseline. Now at 24 weeks after treatment had hearing in the normal range and the second treated patient is following a similar trajectory of improvement through earlier stages of follow-up. We are aiming to enroll several more patients this year, potentially enabling regulatory submissions by the end of next year, and we also look forward to bringing additional auditory gene therapy programs to the clinic in the coming years with the potential to address more common forms of monogenic hearing loss.

Our collaboration with Intellia on CRISPR gene editing continues to advance. We have begun to enroll patients in the Phase III MAGNITUDE study of NTLA-2001 for a lead indication of TTR amyloidosis with cardiomyopathy. The first in vivo CRISPR program clear to enter Phase III studies in the United States. We're also on track to be the first to use CRISPR technology to insert a corrective gene in vivo for a deficiency disease. We have now achieved clearance from both the U.S. and EU authorities for our insertion program for Factor IX, and we have already enrolled initial patients into the leading portion of this program.

Moving on to our siRNA collaboration with Alnylam, which has not only demonstrated successful silencing of genes in the liver, but also for the first time for siRNA in the brain. Additionally, we're excited about potentially initiating later this year a potentially pivotal study for our ALN SOD treatment in ALS patients with SOD1 mutations.

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

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

Thanks, George. Our results in the first quarter demonstrate the strong performance of our commercial portfolio and future growth opportunity. We continue to strengthen and expand our leadership positions across our in-line brands, and we are preparing for potential upcoming launches. I'll start with our anti-VEGF franchise and the ongoing launch progress of EYLEA HD.

First quarter U.S. net sales grew 63% sequentially to $200 million as real-world experience with efficacy and safety continues to grow. EYLEA HD is delivering on its promise of extending the duration between treatments, but the majority of patients achieving this goal. Retina specialists are highly satisfied with EYLEA HD as demonstrated by prescribing across a broad range of patients. To date, most EYLEA HD patients are being switched from existing medicines most notably, EYLEA and faricimab, and we are also seeing an increase in treatment-naive patients.

For the quarter, EYLEA HD and EYLEA together secured 45% of the anti-VEGF category share combined U.S. net sales were $1.4 billion, which includes a reduction in wholesaler inventory of approximately $40 million. This reflects the sequential drawdown of EYLEA inventory that was partially offset by a modest increase in EYLEA HD inventory ahead of the permanent J-code on April 1. Since launch, our team has made significant progress to enhance reimbursement and market access for EYLEA HD. The permanent J-Code has increased prescribers reimbursement confidence, reflected by increased use among existing customers as well as a step-up in new customers ordering for the first time. We're very encouraged by EYLEA HD uptake despite a different payer market today compared to when EYLEA was launched more than a decade ago.

For example, while more than 80% of medical benefit lives are now covered for EYLEA HD increases in utilization management or step edits are impacting all branded products. We are also highly focused on educating patients about the potential for EYLEA HD to deliver best in category vision and safety benefits with fewer injections. In mid-March, we began our direct-to-consumer TV campaign designed to raise brand awareness among treatment experienced and treatment-naive patients. Since initiating the DTC campaign, retina specialists have reported a significant increase in patients actively asking about and being prescribed EYLEA HD. In summary, the EYLEA HD launch outperformed expectations, and we are on track to establish EYLEA HD as the new standard of care for retinal disease.

Turning now to Dupixent. From our first quarter global net sales grew 25% on a constant currency basis to $3.1 billion. In the U.S., net sales grew 17% to $2.2 billion, driven by continued robust demand and the impact of customary first quarter seasonality dynamics, including annual resets

of insurance plans. Dupixent is the clear leader in new-to-brand prescription share across all 5 FDA-approved indications and leads in total biologic prescriptions in 4 of its approved indications.

More than 850,000 patients are currently on therapy worldwide and 3 Dupixent indications have achieved blockbuster status, atopic dermatitis, asthma and nasal polyps. Across all 3 of these indications, Dupixent is competitively differentiated based on its clinical profile, depth of clinical experience and potential to be prescribed to very young patients as young as 6 months in the case of atopic dermatitis.

We continue to see great progress with our recent launches in EoE, Dupixent's GI indication and prurigo nodularis in dermatology. Patient initiations across both indications continue to reach all-time highs and in late January, Dupixent was approved in pediatric EOE, the brand's fourth pediatric indication. Early launch indicators are positive as Dupixent is transforming the standard of care for these children aged 1 to 11 as it has for adults and adolescents with EoE. In addition to its approved indications, there's great potential for Dupixent in an increasing list of additional type 2 diseases, including COPD. If approved, Dupixent will achieve 2 important first, the first biologic medicine for COPD and also the first new treatment in more than a decade for this devastating disease.

In the U.S., approximately 300,000 patients with uncontrolled COPD show evidence of type 2 inflammation. If approved, we will rapidly -- we work to rapidly establish the unique clinical benefits of Dupixent, activate physician adoption, motivate patients to seek treatment and also advance access and affordability. We are confident that COPD will drive meaningful growth for Dupixent, if approved in this indication and see an additional opportunity to address patient unmet need with itepekimab our investigational IL-33 antibody designed to help COPD patients who are former smokers. With significant runway for growth in existing and potential new indications, we are confident in Dupixent's ongoing growth trajectory.

And finally, to libtayo. In the first quarter, global net sales were $264 million, up 44% on a constant currency basis from the prior year, driven by our dual focus in skin and lung cancers. In non-melanoma skin cancer, libtayo continues to lead the immunotherapy category in CSCC and BCC with opportunity for continued market growth. In lung cancer, we are making steady progress in capturing category share in both monotherapy and chemotherapy combination patients. Our oncology team is also preparing for the upcoming August 22 linvoseltamab, PDUFA date recently to reinforces that linvoseltamab has the potential to be best-in-class for late-stage myeloma patients, and we look forward to its potential launch.

In summary, our commercial team continues to bring important medicines to patients across an expanding range of diseases. We are focused on differentiating our medicines to increase category share and drive market growth. Potential upcoming launches across our portfolio provide the opportunity to extend the benefits of our medicines to even more patients. And with that, I'll pass the call to Chris.

Christopher R. Fenimore - Regeneron Pharmaceuticals, Inc. - Senior VP of Finance & CFO

My comments today on Regeneron's financial results and outlook will be on a non-GAAP basis unless otherwise noted. Regeneron delivered solid financial results in the first quarter of 2024. Excluding contributions from our COVID antibodies, total revenues increased 7% year-over-year to $3.1 billion, primarily driven by continued sales growth and margin expansion from Dupixent and strong global sales growth from libtayo. First quarter diluted net income per share was $9.55 on net income of $1.1 billion. Moving to collaboration revenue, first quarter ex-U.S. net sales of EYLEA and EYLEA HD, known as EYLEA 8mg outside the U.S., were $849 million, up 2% on a constant currency basis versus the prior year. Total Bayer collaboration revenue was $356 million, of which $334 million relate to our share of net profits outside the U.S.

Total Sanofi collaboration revenue grew 14% in the first quarter to $910 million. Our share of collaboration profits was $804 million, an increase of 26% versus the prior year, driven by Dupixent's continued volume growth and improving margins. Reimbursement for manufacturing of commercial supply, a component of Sanofi Collaboration Revenues, was $106 million for the quarter, which is expected to be the lowest of the year. On a full year basis, due to higher Dupixent volumes, we expect the amount of these reimbursements to be comparable to 2023.

The Sanofi development balance was approximately $2.2 billion at the end of the first quarter. We anticipate this balance will be fully reimbursed by the end of 2026, which we expect will result in a significant step-up in our Sanofi collaboration profits thereafter.

Before moving to expenses, I will mention that despite lower volumes, U.S. Praluent sales in the first quarter reflected a gross to net adjustment related to a true-up of rebates due to an adverse change in payer coverage. We now expect U.S. net sales of Praluent to be modestly higher in 2024 as compared to 2023, primarily due to this adjustment.

Now to our operating expenses. First quarter R&D expense grew 17% year-over-year to $1.1 billion, reflecting continued investment in our robust pipeline. SG&A grew 13% from the prior year to $544 million in the first quarter, driven by investment to support the launch of EYLEA HD, including direct-to-consumer promotion as well as higher headcount and related costs, primarily for our ongoing international commercial expansion. First quarter gross margin on net product sales was approximately 89%, which was impacted by ongoing start-up costs for our fill/finish manufacturing facility.

First quarter COCM was $193 million, reflecting a decline of 22% compared to the prior year, primarily due to lower Dupixent drug substance manufacturing costs. Now to cash flow and the balance sheet. Regeneron generated $1.4 billion in free cash flow in the first quarter and ended the quarter with cash and marketable securities less debt of approximately $14.8 billion. We repurchased approximately $300 million of our shares in the first quarter and had approximately $1.2 billion available for repurchases under our February 2023 authorization at the end of the first quarter. This morning, we also announced a new $3 billion share repurchase program, which provides us with additional flexibility to continue returning capital to shareholders over time, and we remain buyers of our shares.

Finally, we have made some minor changes to our full year 2024 financial guidance. A complete summary of our latest full year guidance is available in our press release issued earlier this morning. We now expect 2024 R&D expense to be in the range of $4.4 billion to $4.6 billion. The change in R&D guidance is solely due to the inclusion of operating expenses associated with the acquisition of 2seventy bio development programs, which closed on April 1. In summary, Regeneron performed well in the first quarter and is positioned to continue to deliver strong results in 2024 and beyond. With that, I'll pass the call back to Ryan.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - SVP of IR & 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. Josh, can we please go to the first question?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions). And our first question comes from Colin Bristow with UBS.

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

Congrats on the quarter. A question for George. George, there's a lot of interest, obviously, in your muscle sparing obesity program. I was wondering if you could speak to how you think this will differentiate versus competitor muscle-sparing programs and then within that, what will you be specifically paying attention to whenever Lilly decides to disclose the bimagrumab Phase II data?

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

Thanks. Great question. As when you block with other approaches like bimagrumab, you're blocking over a dozen members of the so-called BMP, GDF family and so forth. And that raises the concern because only a couple of those are actually involved in muscle preservation that you may end up doing more harm than good. What we have identified over the years is we identified 2 members of this very large family of almost 20 factors, which 2 are specifically involved in muscle preservation and we created antibodies to each of these 2 individually.

And we're testing these antibodies individually as well as together. And obviously, in this field of obesity, safety matters almost as much as efficacy here. So we believe we have the best program that is testing specifically just the specific members of this very large family that are involved in muscle preservation where they're blocking either one or both together is going to benefit the quality of the weight loss in terms of preserving muscle and maybe even causing more fat loss while creating hopefully the best possible safety profile.

So we think that's a big difference between our program and other programs that are blocking as I said, almost 20 different members that are involved in all sorts of things from growth factors for the bone marrow, for red blood cells, controlling all sorts of things from clotting to liver function and other things and so anyway, that's the major difference in our program.

Operator

Our next question comes from Evan Seigerman with BMO Capital Markets.

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

Kind of a follow-up to Colin. When you think about endpoints in muscle sparing kind of approaches in obesity, what do you think FDA would accept. Right now, they're not really accepting dexa scans, they're just looking at weight loss. Do you think that they would evolve to look at quality of weight loss as a key endpoint asset space evolves?

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

Well, just to remind you, if you look at our paper where we did the nonhuman primate studies and so forth, is the first thing we're going to be looking for is there is the very real possibility of increased weight loss. And that might be the simplest regulatory endpoint of all. After that, if we don't see that, but we see better quality of weight loss, that could be manifested in a variety of ways, though we, of course, recognize that those would perhaps create more complicated ways of being regulated. So obviously, if you increase the fat loss while preserving muscle you should have dramatic benefits in metabolic parameters, which are often used in the field, particularly in people with diabetes and so forth as well as ultimately in terms of function by having maintenance of function as opposed to losing function and maintaining those sort of functional endpoints.

So the simplest path might be simply weight loss one could then move into metabolic parameters or muscle actual functional outcome measures. But to us, the most important thing in the Phase II study is to really just demonstrate the quality of the weight loss in terms of fat versus muscle because ultimately, if you're preserving muscle and increasing the fat loss, it has to be much better for patients, and it may avoid a lot of catastrophic long-term effects of widespread GLP-1 use and so if we see that, we think that we have a real opportunity to turn that into real widespread benefit for patients using this class of drugs.

Operator

Our next question comes from Christopher Raymond with Piper Sandler.

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

I have a question on the EYLEA franchise. I just noticed that McKesson bought one of the largest GPOs, U.S. Retina earlier this year and there's actually been -- as you guys know, a relatively long march of retina practices being rolled up by various private equity firms over the last few years. So I know this is something that's happening across a number of therapeutic specialty areas, but maybe just talk about how you see this phenomenon impacting the practice of ophthalmology in the U.S. and any changes to your go-to-market strategy? And I guess related, the inventory drawdown, we didn't see that happen last year. Was there any effect from maybe some of these changes in your customer base that sort of drove that?

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

Sure. So let me take the inventory item first, and then I'll come back to the overall marketplace. But this was in aggregate. As I mentioned, in the quarter, we saw a reduction in wholesaler inventory broadly of about $40 million. So that reflects market-wide. But that was a combination of 2 elements. It was a sequential drawdown of EYLEA inventory that was partially offset by a modest increase in EYLEA HD inventory ahead of the permanent J-Code on April 1. And then I would share on the overall market in all the categories where we participate, we're always very conscious of the segmentation of the market, targeting the market, what's occurring in terms of customer base and certainly, our strategies and our approach to the marketplace is reflective of that. And the range of customers we have, as you point out, in retina and how that market has evolved over time. And I think our commercialization approach has been very effective in addressing that market evolution.

Operator

Our next question comes from Salveen Richter with Goldman Sachs.

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

With regard to the COPD program here, it doesn't seem like this is an approvability question. So could you just speak to whether restrictions to specific subpopulations could be possible, albeit noting that you had a subpopulation analysis that was consistent with the broader data.

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

Yes, Salveen, thanks for the question. You're right. From our perspective, we think the data broadly supports the entire BLA and as well as all these analyses, the approval of the drug in eosinophilic COPD. As you might imagine, the FDA went anticipating or looking at a new class of biologics is very interested in checking it up and down and down and up and making sure that there's no subpopulation of the study that might be driving the data. So they might -- if one saw that, one might think about labeling it differently, but none of that has occurred. We've looked at all these analyses. We're going to submit them a way ahead of the schedule that they've asked for, and all of the analyses show a consistent and clinically meaningful reduction in the COPD exacerbations across all of these subgroups that have been asked for.

Operator

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

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

For this initial severe food allergy study and the results by year-end, could you elaborate on exactly what will be reported and what you would hope to see to have early clinical proof of concept and how long do you anticipate that these patients would stay on Dupixent in order to maintain low or no IgE levels?

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

These are great questions. We hope from the first few patients if the results are as dramatic as they are in the preclinical studies that we'll be seeing meaningful indicators that we are really reversing severe food allergy. Of course, the first thing and the most important biomarker, as I said, is this evil immunoglobulin IgE, which you can both measure, but they are also routinely tested using these skin prick tests, which are how people are actually evaluated for allergies.

So we expect, first of all, to be seeing that happening in the study in obvious ways. And then we can follow that up, and it is allowed in the study if we see dramatic responses in these markers of the actual allergy-causing immunoglobulin to then go on and do actual food challenges and so forth in the patients. So it all depends on how obvious the reductions in this IgE are and if they are really dramatic, we can go on and do additional allergen-challenged tests. But we hope if the humans behave like the nonhuman primate that we might be seeing something dramatic in the initial patients.

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

George, can you comment? I think they also want to know how long you have to stay on Dupi...

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

Yes. The interesting thing is the animal study suggests that the antibodies against the allergens come back as IgG, G for good antibodies. The whole point of -- if you guys are familiar with so-called immunotherapy or desensitization therapy, all of those therapies, what they're trying to do is induce production of IgG to overwhelm the IgE. That's a much harder thing to do because they're not really getting rid of the Ig. They just have to overwhelm with a lot more IgG. In the animal studies, it suggests that we get rid of the Ig and we replace it with IgG. We don't know, obviously, in the humans, it may be possible that short-term treatment, relatively short-term treatment, may allow patients who have replaced their IgE with IgG, and they will have long-term protection.

On the other hand, we may see that to prevent these patients from making Ig and more IgGs in the future that they may have to stay on the Dupixent for substantial long periods of time. The good news about that as we all know and as was highlighted in Marion's comments, Dupixent compared to most other immunomodulatory agents, it's not immunosuppressive. It actually is corrective for the immune system. And as indicated by its labeling to very, very young patients, it's a very, very relatively safe immunomodulator and biologic. And since most people who have severe allergies also have a lot of other concomitant atopic diseases.

It may be that it is best for these patients to keep their abnormal atopy or abnormal type 2 inflammation under control. So short answer is it's -- there's a possibility it could be relatively short term, but there's also a possibility at least for some or the majority of patients, it could be relatively long term. But the good news is that they may actually have a long-term benefit for the patients because these patients are almost by definition, what you call atopic patients who might need control of their type 2 excess inflammation.

Operator

Our next question comes from Terence Flynn with Morgan Stanley.

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

Just had one on your LAG-3 program. Obviously, you guys are aware that Bristol discussed seeing a signal in a subset of lung cancer that benefits from a combination of PD-1 and LAG-3. So I would just love your latest thoughts on how to think about that in the context of both your program and then what you're hoping to see with this Phase II data later this year?

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

Right. That's a great question. Obviously, the thing that gets us excited about our program compare to the field is that we've seen levels of activity that haven't been seen in the other LAG-3 programs, particularly in melanoma. If that's true in melanoma, there would be hope that this would be seen broadly in other settings and indications. We are certainly excited to see the follow-up details on the BMS story with potential activity in a specific subpopulation that will certainly help point us in our own studies to see what we're seeing within that subpopulation that they are talking about as well as more broadly. But of course, the hope, as I said, is if it is indeed more active in one setting such as melanoma, the hope is it will be broadly more active across other cancer settings as well. So we are excited to see follow-up on their data. We're excited to see follow-up on our data, both in melanoma and in our lung studies.

Operator

Next question comes from William Pickering with Bernstein.

William Pickering - Sanford C. Bernstein & Co., LLC., Research Division - Research Analyst

I had a follow-up on the food allergy program. Could you comment on the dose of linvoseltamab that you'll be testing as compared to the myeloma setting? How -- what gives you confidence in the safety profile and if a patient misses a Dupixent dose, would they then need to start over again with linvo?

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

Yes, these are all great questions. What we've already actually shown based on a variety of studies that we've done is that normal nonmalignant noncancerous plasma cells, the cells that are the immunoglobulin factory cells are the normal versions of the cells are much more susceptible to the bispecific than our malignant myeloma cells. So in discussions and communications with the FDA, we're actually starting at much lower doses than the doses that are used in the myeloma programs, though there is an intra-patient dose escalation process. So we're literally watching -- we're starting with low doses and we're going up in the doses until we actually hopefully see elimination of the IgE. That said, in terms of the safety, I'd just remind you that the much higher myeloma doses, we came up as Len briefly summarized in this program.

We believe that we have a differentiated program in terms of not only efficacy and hospitalization burden and so forth, but also in safety. We have less than 1% Grade 3 events at those high doses in the much sicker myeloma patients. So we hope and we expect that with lower doses in a much healthier population, that this will be a hopefully pretty well tolerated approach. And a much shorter, yes. We think that ultimately, we make it by with a single short course or a very short course of treatment. In terms of whether if somebody takes a holiday, whether one has to then start all over again with the elimination of the IgE cells, we think probably not because it takes a long time to get to those levels of IgE.

So just delaying for a short period of time, we may not bounce back to those levels. As I said, you may have converted all of those cells to IgG or good cellss by that point anyway. But of course, we have to be doing the studies, and we have to be looking at these patients in the clinic to really understand. When I -- I should mention that the Grade 3 events that I was talking about are reflected by cytokine release syndrome. A lot of that is also thought to be -- due to the load of the cancer cells. And obviously, these normal patients have much less of a load here. So it's just another reason to expect, hopefully, better safety. We're going to be going with lower doses, more gentle treatment, and they have much less load in there, so you would expect much less reason to be seeing things like cytokine release syndrome.

Operator

Our next question comes from Carter Gould with Barclays.

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

I wanted to ask another follow-up sort of bispecifics in autoimmune, but I want to go down a little bit of a different path acknowledging the BCMA and Dupi effort. But we've seen sort of CAR-T efforts and ADC approaches sort of come to the rise in lupus and other autoimmune disorders and naturally, people have then started talking about T cell engagers. This seems like a natural place where Regeneron could leverage its bispecific capabilities, expertise. Are there efforts underway internally on this front? Has Regeneron looked at ways to leverage in that expertise?

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

That's a phenomenal question. And first of all, let me remind you that with our long-term collaboration and recent acquisition of 2seventy. 2seventy had exactly the sort of CAR-T programs that you're referring to in lupus and other autoimmune settings, which we are now obviously pursuing together with them but that is one of the reasons why we were excited about turning the collaboration into a situation where we brought all the expertise and the scientists and leadership from 2seventy in-house because we're doing exactly what you suggested. We're hoping to actually literally look in side-by-side studies, how CAR-T approaches in these settings of autoimmune, severe autoimmune disease like lupus and so forth, compare directly head-to-head to our bispecifics. And as you are sort of suggesting, you would think that there would be really little reason to think that the CAR-T solutions would be preferable in this setting, both in terms of off-the-shelfness and the ability to eliminate the normal cells.

As I said, it's usually a lot easier to get rid of normal cells than it is malignant cells. So whatever advantages you might have in certain settings of CAR-Ts you would think in the normal disease setting or at least normal cells in autoimmune disease settings that bispecifics might be just as good, much more convenient and much safer. So together with now our internal Regeneron cell medicines group that has involved a lot of the expertise and leadership of 2seventy, we're exploring that exact question.

I should also say that as clearly been announced by the company and is available in our public disclosures, we have already initiated separately a variety of studies looking at our bispecifics to decrease autoantibodies and autoimmune diseases in other settings as well. So we were already looking at this, but now we're looking at these in direct comparison to our CAR-T approaches with our now internal Regeneron cell medicines efforts.

Operator

Next question comes from Brian Abrahams with RBC Capital Markets.

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

Congrats on all the progress. I know docs are really excited for Dupi and COPD, but it is a new space for biologics. So I'm curious, the amount of education you think is going to be required and how this might affect the initial uptake trajectory. And then how you're thinking the introduction of other biologics, which have also been showing promise might impact the overall long-term market here in Dupi's positioning?

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

So certainly, we look forward to the potential launch of Dupixent in COPD. There's such unmet need and such opportunity to help those patients with an eosinophilic COPD. Our team, as you know, is very experienced with launches in Dupixent. So work is very much underway at Regeneron and also with, obviously, under our collaboration with Sanofi to make sure that we apply the best practices and launch of new indications.

I will share that many of these physicians have already experienced use of Dupixent with tremendous results. We've made great progress, as you know, in asthma leading in new scripts and certainly making tremendous overall performance strides. But we will be very thoughtful on how best to reach physicians, how to make sure that we're aligned with reimbursement and affordability for patients, educating in the way we've come to understand is best for Dupixent in the various markets and indications that we've entered. So we look forward to this opportunity.

Operator

Our next question comes from Mohit Bansal with Wells Fargo.

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

I have a question on itepekimab so in our conversation and literature search, it suggests that there may be a potential for disease modification with some kind of air remodeling at this mechanism. Just wanted to see if you think that is possible? And what markets would you be looking forward to in the Phase III trial beyond exacerbation when the data come.

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

Well, there's always the possibility of disease modification. We actually believe, for example, Dupixent in asthma may be doing exactly that sort of benefit. One of the best ways of actually looking at that is looking at overall loss of lung function over time because, as you know, in these lung diseases as Marion said, in both asthma and COPD, these are diseases of the lungs followed largely by pulmonologists, the same sort of doctors and it is well known that in both of these diseases over time, patients start permanently losing lung capacity and lung function. We are and have been and have early data suggesting that Dupixent may prefer that in asthma, and we'll certainly be looking at those sorts of things for not only Dupixent but itepekimab in the COPD patients in terms of modifying disease and long-term preservation and prevention of this otherwise unstoppable lung function loss.

Operator

And our last question comes from Chris Schott with JPMorgan.

Unidentified Analyst

This is Taylor on for Chris Schott. So we were wondering, would you elaborate a little bit more about how you're thinking about the linvoseltamab launch as we approach the August PDUFA and then thinking about the field more broadly in myeloma, how are you thinking about MRD negativity as a surrogate and thoughts on how you might be able to move into earlier lines in myeloma faster?

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

Marion can take the question on the launch and everything. I mean, obviously, the MRD negativity as endorsed by that panel gives an opportunity to get these kinds of drugs to patients earlier in a variety of settings. So we are looking forward to applying that approach in our future studies as we move towards earlier in different lines of therapy. Marion on the launch?

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

Sure. So we're certainly preparing for the potential launch with the August 22 PDUFA date. And we're really excited because as I've mentioned before, the recent data reinforces linvoseltamab as potentially a best-in-class product for late-stage myeloma patients. So it's a wonderful opportunity to extend our oncology franchise in the new disease area.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - SVP of IR & Strategic Analysis

All right. Thanks, Len and Marion, and thanks to everyone who dialed in 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 IR team here at Regeneron is available to answer any remaining questions that you may have. Thank you once again, and have a great day.

Operator

Thank you. This concludes the conference. Thank you for your participation. You may now disconnect.

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