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REGN.OQ - Q4 2023 Regeneron Pharmaceuticals Inc Earnings Call

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Welcome to the Regeneron Pharmaceuticals' Fourth 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, Senior 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 fourth quarter 2023 earnings conference call. An archive and transcript of this call will be available on the Regeneron Investor Relations website shortly after the call ends.

Joining me today 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; Bob Landry, Executive Vice President and Chief Financial Officer; and Chris Fenimore, Senior Vice President and Controller.

As many of you already know, Bob will retire from Regeneron after our Form 10-K is filed next week, and Chris has been appointed to become Regeneron's next CFO upon Bob's retirement. After our prepared remarks, the remaining time will be available for your questions. We anticipate today's call will last approximately 60 minutes.

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I'd 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-K for the year ended December 31, 2023, which we expect to file with the SEC on Monday, February 5. 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 earnings results press release and our corporate presentation, both of which can be accessed on the Regeneron Investor Relations website. Once our call ends, Bob, 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. Len Schleifer. Len?

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

Thank you, Ryan, and thank you to everyone joining today's call. Fourth quarter 2023 capped another strong year for Regeneron and Bob will walk you through our financial results. For my remarks today, I'd like to briefly look back at 2023 and then discuss what's to come in the year ahead.

2023 was another remarkable year for Regeneron, highlighted by several significant achievements that better position the company to deliver sustainable growth and long-term shareholder value. At the start of the year, we identified 5 key strategic imperatives. First, obtaining FDA approval and successfully launching EYLEA HD. We did encounter a minor delay when we received the complete response letter in late June due to an issue at a third-party filler, but this was quickly remedied and EYLEA HD was granted approval in mid-August.

With what we believe to be a best-in-class potential clinical profile, EYLEA HD is poised to become the new standard of care for patients with wet age-related macular degeneration and diabetic eye diseases. The launch is off to a great start, which Marion will discuss in a few minutes.

Second, we had to defend our intellectual property related to EYLEA. We presented our best case and prevailed in the District Court, which found that one of EYLEA's formulation patents was both valid and infringed by a biosimilar aflibercept manufacturer. This favorable decision may have broad implications and could result in a delay to biosimilar aflibercept launches.

Third, we and our collaborator, Sanofi, needed to continue driving Dupixent growth not only by further penetrating previously approved indications by also reaching even more patients suffering from other diseases driven by Type 2 inflammation. In 2023, we did both. Dupixent global net product sales grew by 34% on a constant currency basis to $11.6 billion. Dupixent led in new-to-brand prescription share in the United States across all 5 of its approved indications.

We also had a major breakthrough in chronic obstructive pulmonary disease or COPD. In March, we reported strong data from the BOREAS study, which enrolled COPD patients with uncontrolled moderate-to-severe disease and evidence of type 2 inflammation. The FDA granted breakthrough therapy designation during the summer but required additional evidence of efficacy to support a regulatory filing. Based on this feedback, we and Sanofi decided to conduct an interim analysis on the replicate NOTUS study, which read out similarly compelling results, enabling our December sBLA submission and a potential U.S. launch for this indication as early as mid-2024.

Fourth, we continued making progress toward our long-term goal of becoming a global leader in oncology. 2023 was highlighted by our regulatory submissions for linvoseltamab, our BCMA by CD3 bispecific in myeloma, and odronextamab, our CD20xCD3 bispecific in lymphoma, while continuing to advance other opportunities in solid tumors.

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And finally, we needed to advance our early-stage pipeline. And over the course of 2023, we presented intriguing proof-of-mechanism or proof-of-concept data across hematology and genetic medicines as well as other areas, including obesity with data from non-human primates. Many of these early programs, which George will run through in a few minutes, represent first or best-in-class opportunities that we believe can drive long-term growth for Regeneron.

Accomplishments in 2023 have put us in a position of strength entering 2024. For this year, one of our strategic imperatives is to continue driving commercial execution, especially the ongoing launch of EYLEA HD, with the goal of accelerating the pace of conversion from other anti-VEGF agents.

Another important launch milestone was achieved last month when the Center for Medicare & Medicaid Services assigned a permanent J-Code for EYLEA HD that will go into effect on April 1, 2024, at which point a potential reimbursement concern for physicians will be removed. We also need to continue to drive Dupixent growth in its currently approved indications as well as from the potential FDA approval and launch in COPD with an eosinophilic phenotype. If approved, Dupixent would represent the first meaningful advance in over a decade for the 300,000 patients in the United States suffering from this form of COPD and would be the first ever biologic approved for COPD.

In oncology this year, aside from continuing to build on the success of Libtayo in non-melanoma skin cancers and non-small cell lung cancer, we are excited about the potential launches of odronextamab and linvoseltamab, the latter of which has the potential to be the best-in-class bispecific for myeloma.

We also expect to make significant advances across our pipeline in 2024, with key readouts for fianlimab, our LAG-3 antibody in combination with Libtayo in metastatic melanoma and non-small cell lung cancer. Libtayo in adjuvant cutaneous squamous cell carcinoma and our Factor XI antibodies in thrombosis, which may inform pivotal studies.

We also plan to initiate clinical trials in obesity, geographic atrophy, hemophilia B and severe food allergies, in addition to expanding early studies of our CD28 co-stimulatory bispecific programs in solid and hematologic malignancies.

In closing, we had a strong 2023 and are poised to deliver in 2024 and beyond. Our pipeline of over 30 clinical programs is delivering important and differentiated innovations. Our commercial team is executing well. And we continue to look at ways to efficiently deploy capital to drive shareholder returns over time.

Before I hand it over to George, I want to take a moment to thank Bob Landry for his many contributions to Regeneron over his 10 years as our Chief Financial Officer. In addition to helping fortify Regeneron's financial strength and discipline, Bob has been an incredible mentor to many of Regeneron's current and future leaders, helped drive our financial results over the past decade, and worked tirelessly to ensure we have the resources needed to help improve the lives of patients around the world. Bob, on behalf of the entire Regeneron family, thank you, and we wish you continued good health and happiness.

As we first announced back in September upon Bob's retirement next week, Chris Fenimore will become the CFO of Regeneron. We all look forward to working closely with Chris in his new role, knowing he brings a similar rigor and depth of financial knowledge that will ensure continuity and collaboration across the organization.

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

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

Thanks, Len. That was really an impressive overview, I have to say.

2023 was another year of firsts delivered by Regeneron, as well as together with our collaborators, all of which have the potential to change the practice of medicine. Starting with inflammation and immunology. As you heard from Len, we are planning yet another launch for Dupixent, this time in eosinophilic COPD, which would represent the sixth disease that this remarkable medicine is approved to treat, and the fifth for which it

would be first in class. Dupixent's transformative potential in COPD is based on the unprecedented results from our first Phase III trial, BOREAS, which were then confirmed by our second Phase III trial NOTUS, demonstrating that Dupixent treated patients had a 34% reduction in the annualized rate of moderate, severe COPD exacerbations.

(technical difficulty)

IL-33 blocking antibody, the pivotal AERIFY-I and II studies passed an interim futility analysis last year. The studies are now on track to complete enrollment in 2024 with an anticipated readout in 2025. If the Phase III results from these studies even approach the Phase II data reported in former smokers, where a 42% reduction in annualized exacerbation rate was observed, itepekimab has the potential to further transform the treatment paradigm for COPD.

Later this year, we are planning on testing an innovative new treatment approach for severe food allergies using a combination of transient BCMAxCD3 bispecific intervention in patients receiving Dupixent therapy. As many of you know, allergic responses are driven by pathologically high levels of the immunoglobulin E or IgE. This is why many say the E in IgE stands for evil. About 40 years ago, it was discovered that interleukin-4 and interleukin-13 were the switch factors required for switching to IgE production.

Based on exciting preclinical data, including in nonhuman primates, as well as human data, our innovative approach has the potential to reverse severe allergies by, first, eliminating the long-lived plasma cells that serve as an IgE reservoir with the BCMAxCD3, followed by blocking of de novo immunoglobin class switching to IgE with the Dupixent.

We are looking forward to starting a small proof-of-concept study, which will inform next steps for this program. We believe this approach has the potential to benefit the millions of people suffering from severe allergies who are at constant risk, as tragically highlighted just last week by the widely reported death of yet another young person unknowingly exposed to a food allergen.

Moving to oncology. Libtayo is the leading PD-1 antibody for non-melanoma skin cancers, including metastatic cutaneous squamous cell carcinoma, or CSCC, and basal cell carcinoma. We are looking forward to potentially expanding the currently approved CSCC indication to include adjuvant CSCC. And we expect results from potentially pivotal interim analysis in this setting in the second half of the year.

Regarding Libtayo combinations, our most advanced is the combination with our LAG-3 antibody, fianlimab. As a reminder, our early clinical data in 3 separate first-line metastatic melanoma cohorts demonstrated potential for best-in-class efficacy when compared cross trial with the approved anti-LAG-3 PD-1 combination product, highlighted by objective response rates greater than 60% and estimated median progression-free survival of longer than 15 months. These early clinical data suggested that the Libtayo fianlimab combination may be one of the most exciting examples of a checkpoint inhibitor combination with clinically meaningful benefit and with the safety profile that is similar to that seen with anti-PD-1 monotherapy. We are expecting a potentially pivotal initial readout from our first-line metastatic melanoma trial by the end of this year. We also anticipate Phase II data in non-small cell lung cancer in late 2024.

On to bispecifics, starting with solid tumors. In the dose escalation trial of our EGFR by CD28 costimulatory bispecifics combined with Libtayo, we have observed promising activity in microsatellite stable colorectal cancer with higher doses of the costim. In terms of safety, so far, we have not seen an increase in immune-related adverse events with this costim. Based on these encouraging early data, which will be presented at a scientific forum later this year, we will be initiating expansion cohorts across several solid tumors in the first half of the year. In 2024, we are also planning to provide updates for our MUC16xCD3 and MUC16xCD28 program in advanced ovarian cancer.

Next, our bispecific for hematology oncology. For linvoseltamab, or BCMAxCD3 bispecific for multiple myeloma, FDA acceptance of our BLA submission is expected later this month. And the EMA recently accepted our MAA submission. These submissions were supported by a potentially best-in-class profile in late-line myeloma in terms of efficacy, safety, dosing, as well as convenience. A confirmatory Phase III study as well as studies in earlier stages of myeloma and premalignant disease are enrolling or will soon begin enrolling patients.

For odronextamab, our CD20xCD3 bispecific for non-Hodgkin's lymphoma, the FDA decision for our BLA is expected by its March 31 PDUFA date, and the EU decision is expected in the second half of the year. In terms of additional recent news for our oncology and immunology pipeline, this

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week, we announced the formation of Regeneron Cell Medicines unit, and that we are acquiring full development and commercialization rights for 2seventy bio's pipeline of investigational immune cell therapies.

We have worked with 2seventy since 2018 on many of these programs and are excited about the opportunity to continue advancing our collective efforts. After deal closing, certain 2seventy employees will join Regeneron Cell Medicines and continue to work on addressing cancer and other serious diseases in novel ways, including by combining Regeneron's antibody capabilities with CAR-T therapies.

Moving from immunology and oncology to obesity and metabolic diseases. Despite all the enthusiasm surrounding GLP-1 agonist for obesity, it has been increasingly recognized that the profound weight loss is accompanied by substantial muscle loss, accounting for up to as much as 40% of the weight loss. This potentially irretrievable muscle loss can be catastrophic for patients and may even lead to major public health concerns in the future.

We have previously shown that our antibodies targeting myostatin and Activin A have the potential to preserve and grow muscle in human trials. Based on these data as well as additional data in obese nonhuman primates, we believe that inhibiting these pathways on top of GLP-1 receptor agonism, has the potential to achieve comparable overall reductions in body weight but with improved quality of the weight loss, resulting in more fat loss while preserving or actually increasing muscle mass.

In mid-2024, we plan to start our first clinical trial to evaluate the combination of our muscle preservation antibodies in combination with semaglutide. Also in 2024, we are anticipating proof-of-concept data for a Factor XI antibodies in the setting of prevention of venous thromboembolism after knee replacement surgery. Based on preclinical and healthy volunteer data, our antibody approach demonstrated more complete Factor XI blockade compared to competing approaches in development for coagulation disorders. And the program is on a rapid path to a registrational trial starting late this year or early next year.

We'll now conclude with our efforts in genetic medicines. Our siRNA collaboration with Alnylam has demonstrated successful silencing of genes in the liver and for the first time for siRNA, in the brain. Proof of principle was achieved for ALN-APP last year and we are anticipating additional data from that program this year, including from patients who have received multiple doses. Based on the success, we are looking forward to new siRNA programs targeting CNS diseases entering the clinic this year, such as ALN-SOD for ALS patients with SOD1 mutations.

Our collaboration with Intellia on CRISPR gene editing continues to advance, where we together produced the first example of CRISPR-based gene editing of a pathological gene in human beings. This initial program for our lead indication of TTR amyloidosis with cardiomyopathy is now in the first in vivo CRISPR program clear to enter Phase III studies in the United States.

Together with Intellia, we also hope to be the first to use CRISPR technology to insert a corrective gene for deficiency disease. We recently achieved IND clearance for our CRISPR-based gene insertion program for Factor IX and initiated the lead-in portion of a clinical trial to evaluate it as a potential cure for hemophilia B.

Moving to genetic hearing loss. We were the first U.S.-based company to announce hearing restoration in a young child suffering from genetic hearing loss after treatment with our novel gene therapy approach. We are excited by these early results for this ultra-rare disease and look forward to advancing to the clinic additional programs potentially address more common forms of monogenic hearing loss. These data represent validation of our viral-based gene therapy program, in this case, locally delivered to the cells of the inner ear.

Beyond these efforts, we have made significant investments in leveraging our monoclonal and bispecific antibody expertise to use these agents to systematically deliver virally based genetic-based payloads directly to specific tissues in the body non-amenable to local delivery, such as to muscle and the central nervous system. Based on encouraging preclinical data, we will be progressing these approaches to the clinic in the coming years.

Finally, concluding with another notable first-in-class program involving a combination of an siRNA with an antibody, in this case to block the C5 complement target. Normally, one needs very high levels of infused antibody to achieve sufficient efficacy because of high target levels regarding C5. But our siRNA cotreatment dramatically lowers C5 target burden, allowing lower and more convenient antibody dosing. We recently shared

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encouraging initial data from a Phase III study in patients with PNH, which supported our hypothesis that this combination approach could provide better efficacy and control of breakthrough hemolysis with more convenient dosing.

Based and building on these data, we continue to enroll our Phase III studies in PNH and myasthenia gravis. We're also planning to extend this combination approach to geographic atrophy and dry AMD. While this combination is expected to have manageable systemic toxicities, including elevated risk of infections, we believe that our approach has several potential advantages over recently approved complement inhibiting agents for GA, which are delivered directly into the eye and have resulted in rare but serious cases of retinal vasculitis, sometimes resulting in permanently impaired vision.

In conclusion, Regeneron's R&D engine continues to grow and deliver many firsts, including differentiated early, mid- and late-stage opportunities, and we are looking forward to additional progress in 2024.

Before I turn the call over to Marion, I would like to add my thanks and appreciation to Bob for his many years of devoted efforts and leadership, and welcoming and look forward to adding Chris Fenimore to our leadership team.

With that, I will turn it over to Marion.

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

Thanks, George. Our business delivered strong results in the fourth quarter and for the year. Over the course of 2023, we successfully launched EYLEA HD, grew Dupixent across approved type 2 inflammatory diseases and expanded Libtayo's presence in lung and non-melanoma skin cancers. We look forward to several potential approvals this year in new therapeutic categories, including in COPD with Dupixent and hematologic oncology using new treatment modalities.

I'll start with our retinal franchise. In January, we announced fourth quarter combined U.S. EYLEA HD and EYLEA net product sales of $1.46 billion. In its first full quarter, EYLEA HD net product sales were $123 million, based on growing demand and positive early physician experience. EYLEA HD is already being used across a broad range of patient types, including those switching from EYLEA, other branded agents, or Avastin, as well as modest but increasing use in treatment-naive patients.

In the fourth quarter, EYLEA HD and EYLEA together secured 49% of the anti-VEGF category share, despite increasing competition and changing market dynamics. This share gain was driven by the differentiated efficacy and safety profile of our medicines as well as a short-term disruption in compounded Avastin due to a quality issue at a large supplier that has since been resolved.

Since launch, we have made significant progress in securing access and reimbursement for EYLEA HD. More than 2/3 of eligible lives are now covered, with the vast majority having first line or single step edit access. Medicare fee-for-service, which represents approximately 45% of total category use, claims are being paid across 100% of jurisdictions using a miscellaneous J-Code.

Looking ahead in 2024, we remind you that the first quarter is typically impacted by payer reauthorizations and that EYLEA HD will remain subject to a miscellaneous J-Code. However, in late January, we achieved another important launch milestone with CMS's assignment of a permanent J-Code for EYLEA HD that will go into effect on April 1. This will provide additional reimbursement confidence for those physicians hesitant to prescribe before a permanent J-Code based on their negative experiences with other new eye disease medicines.

Overall, we are very excited about the future of our retinal franchise. We continue to see physicians prescribe EYLEA HD in both treatment-experienced and treatment-naive settings as EYLEA HD is increasingly recognized as the new standard of care.

Now to Dupixent, where fourth quarter 2023 global net sales grew 31% on a constant currency basis to $3.2 billion and U.S. net sales grew 28% to $2.5 billion. With more than 800,000 patients on therapy worldwide, Dupixent is one of the most important biologic medicines for patients across the spectrum of diseases. Additionally, it continues to have significant growth potential based on new and upcoming indications.

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In the U.S., Dupixent leads new-to-brand prescription share across all 5 approved indications, an important leading indicator for future growth. In addition, Dupixent already leads total prescription share in 4 or 5 approved indications and we are approaching share leadership in biologic asthma.

In atopic dermatitis, Dupixent's largest indication, physicians continue to prescribe Dupixent as a therapy of choice. Despite increased competition over the course of 2023, fourth quarter Dupixent new-to-brand prescription share in AD modestly increased sequentially compared to the third quarter 2023, driven by its differentiated mechanism of action, clinical results and trusted safety profile, including approval in patients as young as 6 months of age.

Dupixent's U.S. label was recently updated with efficacy and safety data for patients with moderate to severe hand or foot atopic dermatitis. Dupixent is the only biologic medicine with data in the label supporting use for this subset of patients with this hard-to-treat disease.

Beyond atopic dermatitis, growth also continues in asthma and nasal polyps, both of which are already blockbuster indications. The recent launches for eosinophilic esophagitis, known as EoE, and prurigo nodularis further contributed to Dupixent's performance and represent indications of significant growth potential. In EoE, which prior to Dupixent's approval had no FDA-approved treatments, nearly 25,000 patients in the U.S. alone have already initiated therapy on Dupixent. The FDA's recent approval of Dupixent in pediatric EOE extends this indication to patients as young as 1 year of age, where approximately 20,000 children in the U.S. being treated for EoE with unapproved therapies. Patient initiations also continue to accelerate in prurigo nodularis, solidifying Dupixent as the standard of care for multiple dermatologic conditions.

In summary, Dupixent is delivering on its potential as one of the most important biologic medicines of our generation with significant remaining opportunity for growth. We anticipate bringing Dupixent to many more patients this year across approved indications. The pediatric EoE launch is already underway, and we are actively preparing to launch Dupixent in eosinophilic COPD pending potential FDA approval later this year.

And finally, to Libtayo. Fourth quarter global net sales grew 43% year-over-year on a constant currency basis to $244 million, with U.S. net sales of $155 million. Libtayo continues to lead the category in non-melanoma skin cancers, and we've made progress in penetrating the non-small cell lung cancer market. In 2024, we expect continued growth across all indications, advancing our goal to exceed $1 billion in annual Libtayo net sales. In conclusion, 2024 provides the opportunity to further build Regeneron's market-leading positions with our medicines across even more therapeutic areas.

Now I'll 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 ended 2023 with strong performance in the fourth quarter. Excluding contributions from Ronapreve, total revenues increased 14% year-over-year to $3.4 billion, primarily driven by sales growth and margin expansion from Dupixent, the launch of EYLEA HD, and strong sales growth from Libtayo. Fourth quarter diluted net income per share was $11.86 on net income of $1.4 billion.

Moving to collaboration revenue and starting with Bayer. Fourth quarter 2023 ex U.S. EYLEA net product sales were $890 million, up 4% on a constant currency basis versus the prior year. Total Bayer collaboration revenue was $377 million, of which $345 million related to our share of EYLEA net profits outside the U.S.

Total Sanofi collaboration revenue grew 19% in the fourth quarter of 2023 to $993 million. Excluding a $50 million sales milestone recorded in the fourth quarter of 2022, Sanofi collaboration revenue grew 26%. Our share of collaboration profits was $886 million, an increase of 43% versus the fourth quarter of 2022, driven by Dupixent's continued volume growth and improving margins.

Reimbursements for manufacturing of commercial supply, a component of Sanofi collaboration revenues, declined 36% versus the prior year due to the implementation of a new higher-yielding manufacturing process. At the end of 2023, the Sanofi development balance was $2.33 billion, reflecting a net decrease of $534 million compared to the balance as of December 31, 2022. Recall, this decrease is primarily recorded as a reduction

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to our share of collaboration profits. We continue to expect this balance to be fully reimbursed in the next few years, which would result in a significant step-up in our Sanofi collaboration profits.

Other revenue was $213 million in the fourth quarter of 2023, up 66% versus the prior year, primarily driven by higher royalties from Novartis on sales of ILARIS and an increase in our share of Arcalyst profit from Kiniksa. The increase in other revenue also reflects higher reimbursements for increased shipment volumes of ex-U.S. commercial supplies of Praluent to Sanofi.

Moving now to our operating expenses. Fourth quarter 2023 R&D expense grew 13% year-over-year to $1.03 billion, which reflects continued investment in our growing pipeline. R&D growth was primarily driven by higher headcount and related costs, funding of our advancing late-stage programs and increased clinical manufacturing activity. SG&A grew 7% from the prior year to $622 million in the fourth quarter, reflecting higher headcount and related costs and higher commercialization expenses, including costs to support the launch of EYLEA HD and prelaunch activities for an anticipated 2024 hem/onc product launches. Fourth quarter COCM declined 12% from the prior year quarter to $210 million. Recall that we are reimbursed for these costs.

Now to cash flow and the balance sheet. In 2023, Regeneron generated $3.9 billion in free cash flow, ending the year with cash and marketable securities less debt of approximately $13.5 billion. In 2023, we repurchased over $2.2 billion of our shares with approximately $1.5 billion remaining authorized for repurchase as of December 31, 2023. Since we began repurchasing our shares in 2019, we have bought back approximately $12 billion worth and are planning to continue to make opportunistic repurchases.

Now moving to our financial guidance for 2024. Note that these guidance ranges do not assume the completion of any business development transactions that were not completed as of today, including our recently announced agreement to acquire preclinical and clinical programs from 2seventy Bio. Starting with R&D expense in 2024, which is anticipated to be in the range of $4.3 billion to $4.5 billion. As George just discussed and as we highlighted at the JPMorgan Conference, our pipeline continues to expand, with a growing number of registration-enabling studies ongoing or expected to initiate this year. These include potentially pivotal studies for fianlimab, Phase III studies in earlier lines of odronextamab and linvoseltamab in our C5 programs.

In addition, we expect to bring 8 to 10 new molecules into the clinic in 2024. We expect 2024 SG&A spend to be in the range of $2.5 billion to $2.65 billion. This reflects increased promotional activities for the ongoing launch of EYLEA HD, investments to support 2 anticipated hem/onc product launches, and higher headcount to support our growing organization inclusive of our ongoing international expansion.

COCM is expected to be in the range of $850 million to $910 million. This range reflects lower drug substance manufacturing costs for Dupixent, offset by higher Dupixent volumes, and higher production costs for other collaboration products, including EYLEA HD for Bayer. Recall, we are reimbursed for COCM expenses and, as a result, we expect reimbursement from Sanofi, which are recorded as a component of Sanofi collaboration revenue, to be slightly lower in 2024 as compared to 2023. We expect the 2024 gross margin on net product sales to be in the range of 89% to 91%. We also expect our effective tax rate to be in the range of 10% to 12%.

Finally, we expect capital expenditures to be in the range of $825 million to $950 million, which reflects expansion of our R&D facilities at our Tarrytown, New York headquarters, as well as continued expansion of our manufacturing capabilities, including ongoing construction of a fill/finish facility in Rensselaer, New York.

In addition to our full year guidance, we expect U.S. net product sales of Praluent to be lower in 2024 as compared to 2023 due to changes in payer coverage. We also expect 2024 net product sales for Inmazeb to be in line with 2023 revenues with nearly all 2024 revenues expected to be recorded in the fourth quarter.

Finally, we anticipate Other Revenue in 2024 to be in line with 2023, with the second half expected to be higher than our first half. Overall, Regeneron performed well in 2023 and our continued investments position the company to drive long-term shareholder value.

Before I conclude, I'd like to sincerely thank Len and George for their kind words. It has been an honor to serve as Regeneron's CFO for these past 10 years, and I have appreciated all of my interactions with each of you in the investment community. I wish Chris Fenimore much success in this

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role and have the utmost confidence that he and the rest of the management team will continue to deliver breakthrough medicines for patients and value to shareholders.

Thank you, and I wish you all continued success. With that, I will pass the call back to Ryan.

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

Thank you, Bob, and congratulations again. 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 1 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 Tyler Van Buren with TD Cowen.

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

Great. And I'd like to say congratulations to you as well, Bob. I wish you well during your retirement. It's been a privilege to work with you. And Chris, I look forward to working with you as well.

So in the opening, Len mentioned accelerating the rate of conversion of patients from other agents to EYLEA HD. So can you discuss the different factors at play that will accelerate the rate over the year, which I assume includes a permanent J-Code and also the robust sampling effort that is impacting 2 mg sales?

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

Sure, Tyler. I'm happy to answer. So as I mentioned, we're very encouraged by the early performance of EYLEA HD in the market, and a number of factors early are driving that success. First, it's the clinical data, which is now showing in the actual market real-world setting the efficacy, safety and durability of EYLEA HD, all very important factors. As we look to the future, physicians will build upon their early experience. And as I mentioned, that experience is coming from conversion patients from branded agents broadly, Avastin, and also, in some cases, naive patients. But going forward, I would share that, in addition to ongoing experience and confidence, the reimbursement consideration is very, very important for physicians, and some are hesitant to prescribe a product that doesn't have a permanent J-Code.

So we do look forward to that occurring April 1 and beyond based on CMS's recent update. And then in addition to reimbursement confidence, we've made progress certainly in payer coverage. We anticipate making more. And certainly, the experience in market to date with EYLEA HD has been very favorable for physicians. And that is, probably, the most important, those differentiating characteristics of the product.

Operator

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

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

Congrats to both Bob and Chris. I was wondering if you could maybe talk a little bit about the differentiation of the emerging obesity portfolio as you move into the next wave of studies. I know a patent filing revealed that the antibody tethered GLP-1 shows very competitive weight loss in animal models. So I'm wondering where you see that differentiating most? Is it tolerability and distribution or dose frequency or somewhere else? And then I know others are pursuing myostatin as well on top of GLP-1s. Just curious where you see your biggest competitive advantage there.

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

Okay. Well, let me start with the latter first, in terms of muscle preservation. Other people have related approaches, but we're the only ones, we're the ones who discovered that there are 2 key ligands or growth factors that control muscle size: myostatin, myostatin 1, we call it, and Myostatin 2 or Activin A. And we're the only ones that have specific blocking antibodies for those 2. And we are testing them together and individually.

And the reason why that's important is it's going to be a combination of both efficacy and safety that matters here. So we're going to see which approach does the best in terms of the muscle preservation in the face of the profound muscle loss that you can see with GLP-1 agonist treatment. But we're also going to see the safety profiles. And I think that, that's going to be so critical because safety is so important here.

Other people are just testing one of these agents alone. I believe, the myostatin and others are testing very broad approaches such as trying to block the receptors for these factors. The problem with the receptor blockade approach is that the receptors that are used by these factors are also used by over a dozen other ligands that have very diverse biologic functions. And you can easily imagine that by blocking so many diverse functions, you might end up having all sorts of safety issues which you're not going to want to be able to be dealing with in the setting of a treatment that's intended to optimize obesity and body weight loss and give benefit to the patients.

So our programs are very different in that we discovered the 2 key regulators, The 2 key growth factors. We have separate antibodies blocking them both. And we're evaluating them separately and together in the setting of GLP-1 receptor agonist, to see what gives us the best benefit vis-a-vis muscle preservation as well as safety profile.

While we're doing that, as we said, we're initiating those trials this year, we are also developing unimolecular solutions. So whichever approach works best, we hope to have the possibility of having a tethered GLP-1, as you put it, associated with the right set of antibody molecules. So they will have the advantage of having a unimolecular solution that can provide all-in-one benefit in terms of providing, hopefully, the best convenience profile and potentially once-a-month dosing, together with providing not only the weight loss, the profound weight loss that one is seen with GLP-1 receptor agonist, but now complemented by providing muscle preservation but with the safest possible approach. So we think that we have the most unique program in terms of addressing all these possibilities. And we're very, very excited about these programs.

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

Thank you, Bob, for all your help over the years. Maybe one question for Marion. Can you just comment on the trends in the anti-VEGF market, underlying trends? I mean, is the market growing or you are growing fast, as fast as it's been in the past, or is it slowing down a little bit? And in that context, how do you see the outlook for high dose EYLEA plus EYLEA going forward, with the underlying demand out there?

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

Sure, Mohit. So there is variation between quarters and years as it relates to anti-VEGF category growth. Overall, though, the category is healthy from a growth standpoint, unfortunately, based on the number of individuals with diabetes or diagnosed with diabetes. On a brighter note, aging

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population is good. So overall, we see it as healthy category growth. But there is variability. And as an example, there has been some decline by a couple of points between last year and this year overall.

Operator

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

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

Maybe just another EYLEA question. I know you guys don't want to get sort of too granular on your pricing strategy, but we've been struck that, even with the 2-milligram format revenue contracting in the last couple of quarters, our checks show that it's really not a market share issue. In fact, share of that format remains up around an all-time high. So one would think that, that's been price erosion that's been driving that.

Just understand this may be a strategy to maximize the HD launch, in broad stroke, can you talk about what we should be expecting in 2024? Do you expect further price erosion for that 2-milligram format? Or have things sort of leveled off?

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

Yes. I'm not sure we want Marion to get into the details of our strategies, pricing, rebates, things like that. But we can say, Marion, you could add thoughts, that we view it as a very competitive marketplace. There has been some price erosion on some of the products in the marketplace. We're starting at a new point with EYLEA HD. We think we priced it well. It was received well. It was intended to match on a yearly basis. And so we think the actual price point was fine.

I don't know if Marion wants to add anything at all but we don't like to comment specifically on those competitive dynamics.

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

Yes. Chris, really nothing in everyone to add to that.

Operator

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

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

And all the best in the future, Bob. Maybe a couple more on the muscle sparing myostatin program. I'm curious, George, what are your thoughts around the potential concerns of myostatin targeting, increases or preserves muscle volume but the muscle is less functional. And then any thoughts on the regulatory pathway that you would utilize for these muscle-sparing assets?

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

Regulatory. Okay. So first of all, we've done extensive work in preclinical models. And these antibodies have already been in humans. We believe that our studies are actually showing that this muscle is functional and certainly very important from both the metabolic and energy expenditure point of view. So, so far, those studies are very supportive of this whole approach.

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I should also say there's a variety of regulatory pathways that we're pursuing here. Obviously, the easiest, which would come from the possible results that we're seeing in the animal studies, is if there's incrementally more weight loss, that might suffice as a regulatory strategy. Alternatively, if it's just the quality of the weight loss, then we would have to show functional outcomes in terms of strength and so forth and so on.

So those are still early in the thinking. We have to see from these initial studies. But as I said, if we simply see increased weight loss, that would be the simplest way forward. And then you have more weight loss but better body composition data, and may also -- may be better metabolic benefits, which we also see in muscle, which could also provide additional paths to approval. So it depends on those results that we're going to get from the initial studies.

I should also mention, in terms of additional programs that we have, obesity. I mean, these are things that are here and now that we're doing these clinical trials and we hope to be getting results over the course of the next year, 1.5 years that could really inform in terms of all these questions that you have and really validate that there's real promise here. But remember, we're doing a lot of other things as well in obesity that are in earlier stages.

So for example, as you probably know, we discovered a brand-new promising target in obesity using our Regeneron Genetics Center, the largest big data set on the planet in terms of human sequence linked to electronic health records, and identified, in some ways, one of the most exciting new targets in obesity that's been ever discovered. And we have a variety, it's called GPR75, it was published in a prominent paper in Science about a year or so ago. And we have a variety of promising and not-that-far-away approaches from the clinic in terms of blocking this target for weight loss. And I think that we presented at JPMorgan early preclinical data using siRNA approaches that look very exciting.

I should also mention that, in terms of smaller programs and so forth, we have things like a very exciting leptin receptor-activating antibody that have had very promising human data as well. So there's a lot of things going on but I think the muscle preservation program and how it goes forward is going to be very interesting to look at over the next year, year-and-a-half.

Operator

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

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

I have one final question for Bob. So Bob, you've done an outstanding job managing the financials of the business and helping drive shareholder returns over the past decade. Looking ahead, how do you believe Regeneron can best use its rapidly growing cash balance to further drive investor returns in the next decade of Regeneron? And thanks for everything, Bob.

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

Evan, thanks for the question, and thanks for the video that we were able to show at my retirement party. It was great.

On that question, George just laid out earlier today, we have so many opportunities with regards to our kind of research and development. And again, I mean I'm going to hand the mantle over to Chris but his #1 priority within capital allocation is to make sure that, that is kind of fully funded. Len and George do a great job with regards to making sure what we're bringing into the clinic has opportunities, and they're going to continue to do that, and there's just a lot coming, particularly when I said kind of 8 to 10 INDs.

Proud on buybacks. Maybe I've kind of circled the victory too much on that with regards to how much we bought back and at what price. But we have a good methodology here that Chris is ingrained with, and he'll continue to do that. And with regards to business development, I mean, just because we can doesn't mean we're going to force something. It has to be right, it has to be a franchise, has to be modalities. You've heard George mention that has to be kind of incremental to what we currently have in the clinic here with regards to RGC and the targets we develop, and all of

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that. So we will remain prudent on that. Continue to be proud of the free cash flow that we're generating. And I trust that Chris, George, Len and the Board will optimize it and put it to great use.

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 Bob, you truly will be missed, and enjoy the next stage of life here. With regard to your GA program, can you outline what's contributing to your confidence in the systemic approach here, and what data you've seen to support it given the move from animal models to Phase III?

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

Okay, geographic atrophy. So basically, the excitement is that, as we show data from our combination approach, we believe that we have the most effective way of blocking the body's C5 activity. The C5, which is active in the eye, is essentially all coming from the liver. And we've shown now in our PNH studies, when we revealed the data from the first portion of our Phase III program, that it looked like we had the best-in-class activity in terms of decreasing the C5 activity.

So if you block it at the source, then you don't have to block it in the eye. And if you block it at the source, then you don't suffer from all the concerns and side effects and so forth that you have from having to block it in the eye. So you block it where it's coming from, then you don't have to treat local in the eye. You can avoid the local side effects.

The concern with systemic blockade is it comes with increased risks of infections and so forth. So we will have to come up with a strategy, which we're working on, to try to mitigate that in the elderly population that suffers from GA. We believe that we may need for that an approach to identify the patients who might be at risk in those settings. Because we certainly know that, for example, patients with PNH and myasthenia gravis who are immunosuppressed and so forth, not only with our agent but certainly with this whole class of agents, can suffer from serious systemic infections when you block C5.

So we are coming up with a way to mitigate that, in part by probably selecting out the patients who are at the highest risk. But in terms of efficacy, the fact that you block it at the source should make it much more effective than trying to block it indirectly in the eye while avoiding all of the serious local side effects you can get in the eye, including this horrific retinal vasculitis, which is associated with sudden and permanent blindness.

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

Thanks, George. I think we have time for 2 more questions.

Operator

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

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

Yes. And first, I wanted to offer my congrats as well and best wishes to you, both Bob and Chris. So I have a commercial question on linvoseltamab, please. It's clearly generated best-in-class results and a more attractive profile for patients. But Regeneron has to displace the incumbents. So could you discuss your plans to convert prescribers to linvoseltamab?

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

Thank you, David. I'm anxious to answer but Len will, of course, go first.

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

No, I just wanted to give a little history, David. You actually were around. You may even have asked the exact question, I'm not sure, when we were launching EYLEA and we had to displace Lucentis by the behemoth Roche. There are some lessons in there that it can be done with starting with a really good molecule, as you described, one that is potentially be best-in-class and then strong execution at the commercial front. We've done it. We're not afraid of the 800-pound gorilla. We hope to put that gorilla on perhaps a weight loss program and get in there and show them what we can do.

Marion, any comments? I just want to put that historical perspective out there.

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

Thank you, David, for the question. And I'm going to be a bit redundant, so I'll be short. But my comment was to say it always starts with the best-in-class molecule. It's about the science. And certainly, you've seen us across therapeutic areas launch into competitive categories, both in the anti-VEGF category and then, more recently, bringing great products into the marketplace. So we do look forward to this opportunity. And it fits quite beautifully with our oncology team, our onc will be onc/hem team. And certainly, we will be very ready for that launch and look forward to helping patients with linvo.

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

Okay. Thanks, Len and Marion. Shannon, last question, please.

Operator

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

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

I'll echo all the prior comments about Bob, and best of luck. Maybe just on the 2seventy deal, Len and George. How should we think about this? Was this more about sort of protecting the rights of the assets that you already kind of partnered on or really around sort of getting access to that manufacturing facility? And does that have implications then as we think about your business development going forward and maybe change kind of your willingness to move further down that path of cellular therapies?

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

I'll let George comment on the scientific rationale, which drives pretty much everything we do. Just to mention from a business development point of view, we have been a long-standing partner with 2seventy when they were still part of bluebird. We've invested in them, both in equity and, frankly, in development. So this was something that was well known.

George can comment how we see this fitting in?

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

Yes. We're excited about the existing programs. But what we're even more excited about is as we know that the history of many diseases but cancer in particular, is about combination approaches. And thus far, even in the setting of this collaboration, the CAR-T space has been separate from the biologics space. And even though we were working together as separate companies, it was a little harder to really move forward in an expedited fashion the incredible opportunities that I believe that we have to combine what we think is the largest and most exciting portfolio of biologics in immunotherapy, together with cell therapy approaches.

Nobody else has really tried that. Nobody else has really led that. Now that we're really together all in with our new selected colleagues from 2seventy and their capabilities, we believe that we will now have the first opportunity to really try this new set of combination approaches against cancer. That is, combining our large portfolio of biologics in the immunotherapy space with their cell therapy capabilities and expertise, that brings a whole new level of combinations to the immunotherapy field. We believe we will be alone in that capability until somebody else tries to copy us and do what we're doing here. And that's what we're really excited about, in addition to just moving forward the existing cell therapy programs that we've been working on them for 5 years or more.

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

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

Operator

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

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