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Regeneron Pharmaceuticals, Inc. (REGN) CEO Len Schleifer on Q3 2019 Results - Earnings Call Transcript

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Q3: 11-05-19 Earnings Summary

Press Release

EPS of $6.67 beats by $0.28 | Revenue of $2.05B (23.14% Y/Y) beats by $66.83M

Earning Call Audio

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Regeneron Pharmaceuticals, Inc. (NASDAQ:REGN) Q3 2019 Earnings Conference Call
November 5, 2019 8:30 AM ET

Company Participants

Justin Holko - VP, IR

Len Schleifer - Co-Founder, President & CEO

George Yancopoulos - Founding Scientist, President, Chief Scientific Officer & Director

Marion McCourt - SVP & Head, Commercial

Robert Landry - EVP, Finance & CFO

Conference Call Participants

Christopher Raymond - Piper Jaffray Companies

Aaron Gal - Sanford C. Bernstein & Co.

Geoffrey Meacham - Bank of America Merrill Lynch

Geoffrey Porges - SVB Leerink

Terence Flynn - Goldman Sachs Group

Matthew Harrison - Morgan Stanley

Yaron Werber - Cowen and Company

Evan Seigerman - Crédit Suisse

Yatin Suneja - Guggenheim Securities

Matthew Holt - JPMorgan Chase & Co.

Joshua Schimmer - Evercore ISI

Operator

Good morning, and welcome to the Regeneron Pharmaceuticals Third Quarter 2019 Earnings Conference Call. My name is Sheryl, 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 Justin Holko. Sir, you may begin.

Justin Holko

Thank you, Sheryl. Good morning, good afternoon and good evening to everyone listening around the world. Thank you for your interest in Regeneron Pharmaceuticals, and welcome to the Third Quarter 2019 Conference Call. An archive of this webcast will be available on our website.

Joining me today on the call are Dr. Leonard Schleifer, Founder, President and Chief Executive Officer; Dr. George Yancopoulos, Founding Scientist, President and Chief Scientific Officer; Marion McCourt, Senior Vice President and Head of Commercial; and Bob Landry, Executive Vice President and Chief Financial Officer. After our prepared remarks, we will open the call for Q&A.

I would also like to remind you that remarks made on this call today 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 competition. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in that statement. A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange Commission, including its Form 10-Q for the quarterly period ended September 30, 2019, which has been filed with the SEC today. Regeneron does not undertake any obligation to update publicly any forward-looking statements whether as a result of new information, future events or otherwise.

In addition, please note that GAAP and non-GAAP measures will be discussed 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 financial results press release, which can be accessed on our website.

Once our call concludes, Bob Landry and the IR team will be available to answer further questions.

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

Len Schleifer

Thanks, Justin. Thanks to everyone who's joining the call today. We had another great quarter, marked by continued execution, to deliver double-digit top and bottom line growth while making progress with our innovative R&D engine. EYLEA global net sales grew 14% to $1.9 billion, including U.S. EYLEA net sales growth of 16% to $1.2 billion. We continued to build on our leadership position in retinal diseases with market share gains across wet age-related macular degeneration and diabetic eye diseases.

DUPIXENT continued to deliver strong growth while transforming the lives of thousands of patients around the world suffering from a number of Type 2 inflammatory diseases. Global net sales of DUPIXENT are now annualizing at more than $2.5 billion. Launches in atopic dermatitis, asthma and chronic rhinosinusitis with nasal polyps are generating broad-based growth for this important brand. We're still in the early days of DUPIXENT as approvals around the world continue and our enthusiasm continues to increase.

Through the strength of the performance of DUPIXENT, we generated improved profitability for our own -- for our antibody collaboration with Sanofi. We expect profits to continue to increase, further diversifying our earnings base driven by growth in DUPIXENT as well as effective cost management across the collaboration.

Importantly, our efforts in oncology are bearing fruit in the form of global launches of Libtayo, our anti-PD-1 therapy in cutaneous squamous cell carcinoma; as well as new data from Libtayo in lung cancer; and our portfolio of innovative bispecific antibodies, including our BCMA antibody in multiple myeloma. We aim to be a leader in immuno-oncology by bringing important new treatments to patients with both blood and solid tumor cancers.

Beyond oncology, we have novel programs that have generated significant late-stage results that we intend to file with regulators, such as evinacumab in homozygous familial hypercholesterolemia. Similarly, results from the PALM study in the Democratic Republic of Congo demonstrated that our antibody combination was superior to the standard of care in preventing death from Ebola in the recent outbreak. We expect further pipeline readouts by the end of the year as George will speak to in a few moments.

Taken together, we continue to demonstrate that Regeneron has the talent and track record to tackle some of the world's most scientifically challenging health issues while creating long-term value for shareholders. We continue to execute on our strategy, and a result -- and as a result, are in a strong financial position. We think carefully about how -- about our capital and how to deploy it strategically.

As such, we will continue to invest in R&D, as we have shown that those investments have generated significant value for shareholders and for patients. Business development efforts will continue as we seek the best science and capabilities to pair with our own

innovations. Beyond R&D, and based upon our confidence in the business to deliver value both in the short and longer term, we are initiating a $1 billion stock buyback program.

These are exciting times for Regeneron. We have strong momentum as we head into the end of the year and into 2020.

Now I'll turn the call over to George.

George Yancopoulos

Thanks, Len. I will begin with DUPIXENT. There is nothing more gratifying than hearing directly from so many individuals about how DUPIXENT changed their lives after years of suffering from diseases such as asthma, atopic dermatitis and nasal polyposis. Just last week, a co-worker shared her story, how she was dreading her fourth surgery for nasal polyposis and instead convinced her doctor to try DUPIXENT. Not only did her nasal polyposis vanish without surgery, but her co-morbid asthma also dramatically improved.

Such stories reflect the science behind DUPIXENT. Many patients suffer from a body-wide hyperactivation of the Type 2 immune pathway, which manifests in disease at many different sites, including the lungs, skin, upper respiratory system and even GI tract. DUPIXENT can be life-changing as it can reverse the systemic Type 2 hyperactivity, thus simultaneously treating multiply apparent, distinct disease entities.

The other remarkable aspect of DUPIXENT is its safety profile. Since Type 2 hyperactivity is often counterproductive, DUPIXENT is not immunosuppressive. Across all of our studies, we have not seen increases in serious infections. In fact, in our AD studies, where people are prone to skin infections, we actually have seen a numeric decrease in infections.

The DUPIXENT opportunity is growing in several ways by expanding to new territories to younger age groups into new Type 2 diseases. For example, the nasal polyposis indication was recently approved by the European Commission. We are submitting for atopic dermatitis in the pediatric population later this year and we are enrolling Phase III studies in eosinophilic esophagitis and chronic obstructive pulmonary disease. In addition,

there are numerous ongoing or soon to be initiated trials in additional Type 2 diseases, including bullous pemphigoid, prurigo nodularis, chronic spontaneous urticaria, hand and foot atopic dermatitis, alopecia areata and allergic bronchopulmonary aspergillosis.

We're also very excited about the potential of DUPIXENT to accelerate and enhance allergen desensitization. Our combination trial with the immunotherapy for grass allergy will be presented at a future medical conference. And data in combination with Aimmune's AR101 for peanut allergy are planned for late next year. Related to our DUPIXENT efforts, we are expecting a readout of our interleukin-33 antibody, Regeneron 3500, in atopic dermatitis and COPD over the coming year.

As you know, DUPIXENT is currently approved for uncontrolled moderate-to-severe asthma and atopic dermatitis and is approved in earlier stages of these diseases. However, because of its efficacy and safety profile, including the lack of immunosuppression, we believe DUPIXENT can have an important benefit earlier in these diseases, where biologics have thus not -- thus far not been utilized. And we are considering studying DUPIXENT in patients with these earlier stages of disease.

Now we'll turn to our immuno-oncology efforts. First, I want to remind you how challenging it is to create best-in-class biologicals and how often failure is still the rule. The foundation for Regeneron's success over the years has been our technology platforms that we have repeatedly used to produce first-in-class or best-in-class biologics, whether EYLEA for eye diseases, PRALUENT for heart disease, DUPIXENT for allergic Type 2 diseases or the recent stunning success with our Ebola antibody cocktail. I need not remind you that in all of these settings, there were very few, if any, successful competitors. Instead, numerous competitors, including some of the biggest biopharma companies in the world, failed. And now we feel that we can create similar advantage by bringing our next-generation technologies to immuno-oncology.

Arguably the biggest advance in this field has been PD-1 blockade. But even here, most efforts to develop PD-1 or PD-L1 blockers have not produced best-in-class results, with Merck's pembrolizumab being a clear outlier. Moreover, even with this best-in-class PD-1

blocker, most cancers do not respond. And for those that do, only a fraction of the patients have satisfactory response. We are very far from curing cancer in general. This is why we feel that with our technological advantages, we can make a major contribution.

First of all, we believe we can use our VelocImmune human/mouse, the widely acknowledged gold standard for making fully human antibodies, to make best-in-class checkpoint blockers such as for PD-1. Moreover, we have developed a next-generation VelocImmune mouse that, when combined with our recently described Veloci-Bi platform can produce the most natural antibody-like bispecifics more rapidly and routinely than other approaches. Our bispecifics naturally have long half lives without complex engineering, without mutations and can be delivered like normal antibodies without requiring constant infusion. This has allowed us to emerge as a leader in the so-called CD3 bispecific space, in which a bispecific can be used to link a killer T cell to a tumor target.

Moreover, we have invented what we believe is the next important class of bispecifics, which we call co-stimulatory, or co-stim, bispecifics that can synergize with both our PD-1 antibody and with our CD3 bispecifics. We believe that progress in cancer will require amplifying and deepening the responses and settings where PD-1 antibody is already active as well as activating responses where PD-1 has little or no activity, such as in prostate, pancreatic, colorectal and other settings. We hope that our bispecifics will demonstrate such synergies together as well as with our PD-1 antibody.

We have already begun establishing the individual efficacy profiles of our 3 classes of immuno-oncology agents. In terms of our PD-1 antibody, Libtayo, we defied expectations by identifying important new cancer setting where PD-1 therapy had not previously been characterized despite the broad efforts in the field. We obtained rapid approval in cutaneous squamous cell carcinoma, or CSCC, based on some of the best response rates yet described for a PD-1 block into a solid tumor setting, approaching 50% in late-stage metastatic and locally advanced CSCC. While others have subsequently explored their PD-1 therapies in this setting, Libtayo remains the first and only approved therapeutic in advanced CSCC, and based on cross-study comparisons, has an outstanding efficacy profile.

We believe non-melanoma skin cancers represent an important previously untapped opportunity, and we are working to expand our leading position in this space. A registrational study in adjuvant CSCC is already ongoing. In addition, Dr. Neil Gross of MD Anderson recently presented exciting early results with Libtayo in neoadjuvant CSCC with 70% response rates and 55% complete pathological responses. And we are now planning a larger new adjuvant study.

We're also looking forward to a potentially pivotal data in the first half of 2020 for another -- from another important common skin cancer where PD-1 therapies have not been extensively characterized. That is basal cell carcinoma. Finally for skin cancers, we're also exploring Libtayo in melanoma in various combination studies intended to show increased benefit over PD-1 therapy alone.

Beyond skin cancers, we are working to establish Libtayo as a therapeutic in non-small cell lung cancer, the largest current PD-1 opportunity. Along these lines, earlier today, we provided an update on our lung study with Libtayo monotherapy in high PD-L1 expressers. This 700-patient study is now over 90% enrolled. Based on an early interim analysis of overall survival in about 1/3 of anticipated events, the IDMC recommended continuing the trial as planned.

We also announced that in the first 361 randomized patients, the confirmed objective response rate as determined by the investigators is currently 42% Libtayo versus 22% for chemotherapy. These objective response findings, while not sufficient for regulatory approval in this setting, support our hope that Libtayo may prove an important therapeutic and non-small cell lung cancer. The next event-driven interim analysis for overall survival is anticipated in 2020.

In terms of other important phase -- in terms of our other important Phase III study in lung cancer, which is comparing Libtayo with chemotherapy versus chemotherapy alone. We expect full enrollment in the second half of next year.

As with our PD-1 antibody, we are also establishing the efficacy and safety profile of bispecifics first as single agents. Starting with our CD3-class of bispecifics, we have already reported that Regeneron 1979, our CD20xCD3 bispecific, demonstrated

impressive single-agent response rates in late-stage lymphoma patients, including in those that have failed CAR-T therapy.

At the European Hematology Association meeting, based on a small number of patients, we reported 93% objective response rates with 71% complete responses in late-stage follicular lymphoma and reported 57% response rates in late-stage diffuse large B-cell lymphoma patients, including 2 responses in 4 patients that had failed CAR-T therapy.

While the ASH abstracts that we'll be posting tomorrow will only include older data, our presentation at ASH will include additional patients in longer duration of follow-up with about 20 patients at effective dose levels for each of follicular lymphoma and DLBCL. We have already initiated a potentially pivotal Phase II study which intends to enroll independent arms with different subtypes of non-Hodgkin lymphoma.

In terms of our BCMAxCD3 bispecific, based on early single-agent proof of concept data that we will present at ASH, we are encouraged about the potential of this treatment for multiple myeloma. Remind you that the abstracts -- the ASH abstract posting tomorrow will also reflect all the data, including only our first dosing level with the BCMA bispecific. We look forward to updating these results with promising new data from our second dosing cohort at ASH.

Finally, our third CD3 bispecific, MUC16xCD3, continues in a trial as a single agent and will shortly start a combination phase with Libtayo. In terms of the first example of our entirely novel class of so-called co-stim bispecifics, our PCMAxCD28 bispecific, we have begun dosing patients in recently initiated combinations with Libtayo. In this prostate cancer setting, which is normally not responsive to PD-1, we hope that our PCMAxCD28 bispecific can trigger responses as it has in preclinical studies.

In summary, we are very excited that the initial entries for our three different classes of immuno-oncology therapeutics are establishing their individual potentials, and we are entering into the next stage, exploring combinations. In terms of combinations, we're not limiting ourselves to our internal portfolio. Our external immuno-oncology collaborations fall into 2 broad categories: Cell therapy, including CAR-Ts and other approaches; and vaccine-like approaches. Once again, these all have the potential of being explored

individually but also in combination with our PD-1 and other checkpoint inhibitors as well as with our 2 classes of bispecifics. Altogether, we believe we are making significant progress on our strategy to become a leader in the immuno-oncology space.

I would like to finish with brief discussions updating our ophthalmology efforts and also briefly touch on our rare disease portfolio. For EYLEA, we are planning registrational clinical programs in wet AMD and DME, evaluating a novel and higher-dose formulation of 8 milligrams in 8-week -- sorry, in 12-week and 16-week regimens. The Phase II trial in wet AMD is underway. Beyond EYLEA, we are continuing preclinical development of a new VEGF blocker, gene therapy and other novel approaches, including with our Alnylam collaborators.

We have also made substantial progress in our rare disease portfolio. In mid-2020, we are planning a regulatory submission for evinacumab in homozygous familial hypercholesterolemia based on Phase III data showing nearly 50% LDL reduction in patients already treated with statins and PCSK9s. By the end of 2019, we're also expecting a readout of garetosmab for fibrodysplasia ossificans progressiva. And we are becoming increasingly excited about our C5 program.

Let remind you, we set a very high bar for entry into existing markets with novel agents. In the case of C5, our goal was to achieve convenient self-administration with a subcutaneous dosage form as well as more complete blockade of inappropriate complement activation. We are encouraged by our progress towards these goals and plan to present our first data for our C5 antibody, pozelimab, in paroxysmal nocturnal hemoglobinuria patients at a future medical conference. We're also exploring options for combination with cemdisiran, a novel SRNA developed by our Alnylam collaborators.

In closing, this is a very interesting time to be at Regeneron. Now we'll turn the call over to Marion.

Marion McCourt

Thank you, George. We continued to execute well in the third quarter led by our core EYLEA and DUPIXENT businesses as well as promising Libtayo market introduction. Starting with EYLEA. Global net product sales grew 14% year-over-year to $1.9 billion. In

the U.S., net product sales grew to $1.2 billion. This represents 16% year-over-year growth. A combination of overall market growth and share gains drove strong third quarter performance of EYLEA. Growth in the overall market continues at a mid- to high single-digit range, underpinned by the aging population and increase in diabetes prevalence. EYLEA's share of the branded market also increased to 73% of net product sales for the quarter driven by physician preference for EYLEA. We continue to invest in EYLEA to advance our market-leading position across all indications.

Let me take a moment to remind you of select strategic commercial initiatives to enhance our market-leading position in wet AMD and further penetrate diabetic eye disease, where there is significant growth opportunity. In wet AMD, we are growing our position by focusing on EYLEA's rapid and sustained outcomes to improve and protect vision. Wet AMD currently represents just under 60% of EYLEA business and EYLEA continues to grow in this patient group. In diabetic eye disease, our expanded field team is making tremendous strides. Our strategy is to increase diagnosis and treatment rates by educating health care professionals, consumer awareness and applying technologies to support diagnosis. With approximately 15% of the market receiving an anti-VEGF treatment, there's an important opportunity to help patients preserve and improve their vision. Our growth in DME indicates our strategy is delivering results.

Our diabetic retinopathy launch is off to an encouraging start, with EYLEA use increasing in both proliferative disease and severe non-proliferative disease. We anticipate EYLEA use to increase as retina specialists see the benefits of actively treating these patients. Finally, we plan to launch the EYLEA prefilled syringe before the end of this year. Taken together, EYLEA has compelling efficacy and safety, breadth of indications, dosing flexibility and clinical and real-world experience.

Turning to oncology. We're commercializing Libtayo with Sanofi. Global net sales of Libtayo were $52 million, including $4 million from our recent ex U.S. market launches that began this quarter. In the U.S., we continue to establish Libtayo as a standard of care across all lines of therapy for advanced cutaneous squamous cell carcinoma, or CSCC. Libtayo is now the #1 systemic CSCC treatment in terms of total patients. It is outperforming chemotherapy and has made rapid share gains within the anti-PD-1 class, where Libtayo has 80% share in new patients. We expect growth to continue based on

demographics, enhancements in patient identification and referrals. In addition, recent updates to the National Comprehensive Cancer Network, or NCCN guidelines, list Libtayo as the preferred single-agent systemic option. Libtayo is the only CSCC, anti-PD-1 treatment with a 2A recommendation. Ex U.S. launches in CSCC are currently underway in multiple markets, including Germany, the U.K. and Brazil. While early, we are seeing encouraging progress on access and reimbursement as well as prescribing trends and physician interest.

Moving to PRALUENT. In the second quarter, global net sales were $70 million. We are working diligently with our collaborator Sanofi to address brand profitability.

Turning to KEVZARA. In the third quarter, global net sales were $55 million. In the U.S., we see steady growth as KEVZARA continues to make headway in the IL-6 subcutaneous class, with 48% share of new-to-brand prescriptions and 30% share of total prescriptions. Now for DUPIXENT, which is transforming the lives of patients suffering from many Type 2 inflammatory diseases. Global net product sales in the third quarter were $633 million. In the U.S., net product sales reached $508 million, representing 131% year-over-year growth. Total prescriptions in the U.S. grew approximately 21% compared to the second quarter. We continue to see strong prescribing trends across all approved indications. Weekly new-to-brand prescriptions for the third quarter averaged approximately 1,350 patients per week, up from 1,200 in the prior quarter.

In atopic dermatitis, DUPIXENT continues to outpace other biologic launches in dermatology. For adults, we are pleased to see an increased number of patients with moderate disease being prescribed DUPIXENT earlier in the treatment paradigm and ahead of immunosuppressant therapy. We see ample opportunity in atopic dermatitis as approximately 20% of adult patients with the greatest need have used DUPIXENT. Additionally, our ongoing launch in adolescents continues to contribute meaningfully to the brand.

As a reminder, DUPIXENT is the first biologic approved for atopic dermatitis in adolescents, many of whom remained uncontrolled using topical therapies. This launch has been aided by physician experience with the efficacy and safety and adults.

In asthma, DUPIXENT in positioned to capitalize on this significant market opportunity. Approximately 75% of DUPIXENT asthma patients are new to biologics, demonstrating our ability to grow this market. Prescribing trends are accelerating among both allergists and pulmonologists. With only 15% of eligible patients being treated with a biologic, there's significant opportunity to educate patients about DUPIXENT. As a result, last month, we initiated our asthma direct-to-consumer TV campaign.

Finally, our launch in chronic rhinosinusitis with nasal polyps is going extremely well. Encouragingly, patients are being initiated on DUPIXENT regardless of prior surgery. As a reminder, in the U.S., up to 90,000 adults with this disease are considered uncontrolled despite prior surgery or systemic corticosteroid use. About 55,000 patients have had prior surgery. While early in the launch, we believe this will be a meaningful growth opportunity for DUPIXENT.

We have an unprecedented opportunity with DUPIXENT in Type 2 inflammatory diseases. The number of physicians prescribing is growing. And with more than 100,000 patients globally treated with DUPIXENT, the outlook remains exceedingly positive.

In closing, the commercial organization delivered a solid performance in the third quarter. We have the right strategy and we are executing to deliver short- and long-term growth.

Now I'll turn the call over to Bob.

Robert Landry

Thanks, Marion. For the third quarter 2019, Regeneron delivered double-digit growth on the top and bottom lines driven by strong performance from both EYLEA and DUPIXENT and increased profitability within the Sanofi Alliance. Total revenues for Regeneron grew 23% year-over-year to $2.05 billion driven by continued growth of our core brands, EYLEA and DUPIXENT. Non-GAAP diluted net income per share grew 14% year-over-year to $6.67 on non-GAAP net income of $762 million.

Since Marion discussed our EYLEA results in the U.S., I will start with our Bayer and Sanofi collaborations. Starting with the Bayer collaboration. Ex U.S. EYLEA net product sales, which are reported to us by Bayer, were $730 million, representing a 12% reported

and a 14% constant currency basis increase year-over-year. Total Bayer collaboration revenue for the third quarter of 2019 grew 15% year-over-year to $303 million, of which $275 million was derived from our share of net profits from EYLEA sales outside the U.S.

Total Sanofi collaboration revenue was $404 million, up 58% year-over-year, as commercial profitability improved sharply. For the third quarter of 2019, Regeneron recognized a profit of $94 million in connection with the commercialization of non IO antibodies compared to a loss of $39 million in the prior year period and a profit of $39 million in the second quarter of this year. Both the year-over-year and sequential increase was driven by higher DUPIXENT profits. As we head into the end of the year and into 2020, we expect continued improved profitability driven by strong DUPIXENT net sales growth, continued cost containment on PRALUENT and KEVZARA and improvements in our operating leverage.

Turning now to expenses. Non-GAAP R&D expenses were $603 million for the third quarter of 2019 compared to $497 million for the third quarter of 2018, an increase of 22%. We are continuing to invest in our pipeline and research capabilities which is critical to the long-term success of the business.

Our oncology pipeline continues to forge ahead, and we are advancing several wholly owned molecules into clinical development with more to come. In addition, we are funding external partnership obligations as jointly developed molecules are rapidly advancing. While we are not yet giving guidance for 2020, we anticipate non-GAAP R&D expenses to increase.

Our non-GAAP unreimbursed R&D expense, which is calculated as the total non-GAAP R&D expense less R&D reimbursements from our collaborators, was $441 million for third quarter 2019 compared to $311 million for the third quarter of 2018. Based on the current forecast for the remainder of the year, we are tightening our previous full year 2019 guidance for non-GAAP unreimbursed R&D to $1.68 billion to $1.71 billion.

Next, non-GAAP SG&A expense was $379 million for the third quarter of 2019, a 16% year-over increase driven by higher headcount and related costs and launch-related expenses for U.S. Libtayo and for new indications for EYLEA and DUPIXENT. We are

tightening our previous full year 2019 guidance for non-GAAP SG&A to $1.55 billion to $1.58 billion.

Sanofi reimbursement of Regeneron commercialization-related expenses, line items found within Sanofi collaboration revenue, was $115 million for the third quarter of 2019. Based on spending trends and cost containment efforts related to PRALUENT and KEVZARA, we are lowering and tightening our previous full year 2019 guidance for Sanofi reimbursement of Regeneron commercialization-related expenses to $490 million to $510 million.

In the third quarter of 2019, combined non-GAAP cost of goods sold and cost of collaboration and contract manufacturing were $210 million compared to $102 million in the third quarter of 2018. The year-over-year increase in cost of goods sold was primarily due to the company's obligation to pay Sanofi its share of Libtayo U.S. gross profits, lower fixed cost absorption and higher inventory reserves and write-offs. The year-over-year increase in cost of collaboration and contract manufacturing was primarily due to recognition of manufacturing costs associated with higher sales of DUPIXENT.

Turning now to taxes. For the third quarter of 2019, our GAAP effective tax rate was 12.9% compared to 6.5% for the third quarter of 2018. Based on our actual results to date and forecast for the remainder of the year, we are raising our full year 2019 GAAP effective tax rate guidance to 12% to 14%. We continue to expect our full year 2019 non-GAAP tax rate to be higher than our full year 2019 GAAP effective tax rate.

Turning next to our cash flow and balance sheet. Year-to-date, we've generated $1.35 billion in free cash flow, defined as net cash provided by operating activities less capital expenditures. We ended the third quarter of 2019 with cash and marketable securities of nearly $6 billion.

Earlier today, we announced a $1 billion share repurchase program. With that announcement, let me take a moment to discuss our capital allocation priorities. In terms of capital deployment, investing in our internal research capabilities and advancing our pipeline remains our top priority. As evident by our productivity and the high returns we've generated historically on our R&D, these investments are critical for our business and shareholders.

Second, we seek to complement our internal efforts with external strategic partnerships and collaborations. Over the last 18 months, we've funded in excess of $900 million in equity and upfront payments, comprising more than 5 new strategic opportunities in the areas of RNAi therapeutics, oncolytic viruses and CAR-T therapies. Following these R&D investments, we assess additional strategic uses of our cash.

Our overall business is growing with increasingly diversified revenue and cash flow streams. Coupled with the strength of our balance sheet and our confidence in the long-term outlook for the business, we view share buybacks at current trading levels as an efficient use of capital.

In conclusion, we are very pleased with our financial results and performance this quarter. With continued execution on our R&D and commercial strategies, we are positioned for long-term growth.

With that, I'd like to turn the call back to Justin.

Justin Holko

Thank you, Bob. Sheryl, that concludes our prepared remarks. We'd now like to open the call for Q&A.

Question-and-Answer Session

Operator

[Operator Instructions]. Our first question comes from Chris Raymond from Piper Jaffray.

Christopher Raymond

So just maybe a question on the EYLEA franchise. And maybe just from a high-level perspective, you guys have been framing your next-generation efforts in a pretty similar way, I think, for a few quarters now. And so the high-dose formulations in the clinic now, which I think is new. But your discussion on the other mechanisms still seem to be framed in the same way that you had the last few quarters.

And so I guess the question is I'm wondering if you can talk about where -- when we might see something from these novel mechanisms in the clinic. And maybe talk about these efforts in the context of the IP runway you have with EYLEA. And then maybe a second part of the question, can you describe more tactically any continued impact from the supply hiccups of compounded Avastin on the quarter?

Len Schleifer

So Marion will take any comments about the Avastin supply issues. Let me just say that -- I'm not going to comment on our patent situation here. I can say one thing for sure, is that our data exclusivity runs some ways into 2024, so we have a reasonable runway there. In terms of timing, obviously, we're working hard. We tend, Chris, not to predict when things will finally go into the clinic. But as soon as they do, we will let you know. We're hard at work at it. And the one that we mentioned, the high-dose, the new formulation, is now underway in our Phase II program. Marion, you want to comment on the Avastin situation?

Marion McCourt

Sure, Len. And just to comment, in the third quarter, there were some temporary spot shortages of Avastin in select geographies, so they may have given some modest benefit to EYLEA. We mentioned the same in the second quarter. And the one thing I can add is that we are hearing that patients that are started on Avast -- excuse me, started on EYLEA because of these shortages do continue on EYLEA therapy. So we'll continue to monitor the situation, which is episodic. And of course, in many instances, are related to ongoing issues with compounding and quality concerns.

Operator

Our next question comes from Ronny Gal from Bernstein.

Aaron Gal

A couple, if you don't mind. First, on the CD3xCD20. George, it looks like you might have actually got here with Roche. Can you comment a little bit about your -- the -- kind of how you differentiate your program from the Marcelin [ph] program, the developed program?

And are you going straight into first line with this? Or are you still thinking it's going to be in a relapse setting for the next set of trial? And if you can remind us whether the partnership with Sanofi gives them the right to enter this program? Or is it still at your control. And given you're now in a kind of an excess cash situation, you have more choice about what you're going to do with this?

George Yancopoulos

Well, maybe I'll start at the back because it's the easiest. It's a wholly owned program that we control and nobody has an option on it. Number one. Number two, in terms of the comparisons with Roche, I mean, obviously, these are cross-trial comparisons. But we're very encouraged with how our data looks and how we both have a -- how we have a chance to have best-in-class potential. One of the most important things, we believe, about not only this program but our immuno-oncology franchise in general, is that we have, we believe, an unparalled opportunity to generate synergistic therapeutics that can work very powerfully together. So we are certainly going to be exploring our CD20xCD3 in combination with our PD-1 antibody, Libtayo, which we're very interested in. But also, we have an assortment of additional bispecifics in the settings where one might need additional efficacy. We believe that we can add to it, and we've certainly shown that and demonstrated that in preclinical models.

So we think that, that's what really differentiates us, is that we really have a lot of tools in our tool kits a lot of possibilities for combining a lot of things with synergistic capabilities together. In addition to the fact that each one of our individual agents, we believe that based on the emerging data, has a chance to be best-in-class. And we're moving very aggressively into a near-term pivotal, approvable trials. And we'll be moving into earlier stages as well.

Len Schleifer

Certainly, it's Len, just to echo what George said. We feel good about our position, but we don't take Roche lightly. They're a formidable -- Roche/Genentech are a formidable competitor with lots of experience in the CD20 space. But they may have historical approaches that may be -- might be disruptible by new agents and combinations.

Operator

Our next question comes from Geoff Meacham from Bank of America.

Geoffrey Meacham

Just have a couple for Bob. I wanted to ask about the commercialization-related expenses. Was this just lower reimbursable expenses to Regeneron? Or is it related to, say, DUPI profitability? Or is this sort of -- should be looked at as the next phase of the JV expense base overall? And then for George. Obviously, you've got Libtayo-chemo combos going and CTLA-4 combos going, but how much of a priority is it to test more novel mechanisms with PD-1, just given recent data from AZ and Bristol?

Robert Landry

Geoff, I'll start. Well certainly, with the launch of DUPIXENT in the new indications, I mean we're moving full speed ahead with regards to that. And we've been talking about PRALUENT and KEVZARA cost containment for the last couple of quarters I would say in the third quarter, you're meaning -- we meaningfully saw what we were -- have been working on with our Sanofi counterparts in terms of trying to rein in a little bit with regards to the amount of OpEx associated with PRALUENT and KEVZARA.

George Yancopoulos

Okay. And so certainly, we're following closely the PD-1 field. As you said, it is evolving. Our goal, as it's been from the beginning, is to have a foundational PD-1 therapeutic that is at least competitive, if not best-in-class. And so we're very excited, for example, about some of the data that we reported on today in terms of the response rates in our first-line monotherapy lung cancer study. But once again, the story is as you said, that we think that we have an enormous opportunity of combining with our novel sets of reagents. Some of which are already in combinations in the clinic not only with the entire assortment of checkpoint inhibitors but also with our entire assortment of bispecifics.

So as I already mentioned, we're exploring combinations with the bispecifics of the CD3 class that are in the clinic already, but we've already initiated our second class of bispecifics, these co-stimulatory bispecifics, which have the opportunity to activate PD-1

responsiveness in tumors that are not normally responsive to PD-1. So not only can they enhance responsiveness in tumors that are responding to some degree already, but they can actually endow responsiveness in those that don't in preclinical models. And we hope that, that pertains, obviously, in the clinic. This creates, we think, a great way of extending the benefit that immuno-oncology has already provided by taking it deeper in cancers that are already responsive, but also opening up cancers that haven't responded to date.

So I do want to just emphasize again, why do we have this ability? Because we have a unique platform for making these bispecifics. As far as I'm aware, we're the only platform that couples essentially a naturally derived bispecific antibodies using a genetically humanized mouse, together with this Veloci-Bi platform that we recently announced, to rapidly and routinely make natural bispecifics that behave just like normal antibodies.

You don't have to give them by constant infusion. You don't have to introduce linkers. You don't have to make mutations in there so that they have longer half-lives because they look, and they're manufactured in fact, just like regular antibodies. They behave like them. You can give them normally like you give biologics. You don't have to go to special -- extensive lengths to manufacture them. This allows us to rapidly and routinely make many of these and put them into the clinic very rapidly in these various combinations and target them in exactly the way we want to, in some cases, initiate; or in other cases, trigger or activate a co-response. And I think it's the collection of these put together that allow for very exciting combinations, as I said.

Len Schleifer

Yes, and let me just add something very quickly. Geoff, you also alluded to there were other combinations out there, whether it be CTLA-4, LAG-3 or what have you. We in this field recognize that not all antibodies are created equally. As George said, I mean, you've got some antibody like a KEYTRUDA that worked in first line; and others, let's say, in PD-L1; or others even in PD-1 that may not work as well, didn't work. And so we have to make sure we explore some of these other antibodies, LAG3 or what have you ourselves, to be satisfied that there's not opportunity for a combination therapy there as well.

Justin Holko

[Operator Instructions]. We still have several callers that we'd like to squeeze in.

Operator

Our next question comes from George -- I'm sorry, Geoff Porges from SVB Leerink.

Geoffrey Porges

A quick question. You have three products that are -- look like they're annualizing at about $200 million a year in revenue: KEVZARA, Libtayo and PRALUENT. And certainly, Libtayo is still growing strongly. First, Bob, can you give us a sense of whether they're actually contributing to cash flow at that revenue level? And secondly, do you envisage any further changes in the commercial support, the structure behind those products, such that they could enhance the profitability or at least not drag on the profitability of DUPIXENT in the future?

Robert Landry

Geoff, I'll start. And you can imagine for competitive reasons, we're not going to get into kind of specific products with regards to what they're generating from a cash flow perspective. We've given kind of high-level cover -- color with regards to what the drivers have been. Obviously, DUPIXENT on our current profitability for the quarter. Repeat the second question, the second part of it.

Geoffrey Porges

Yes. Are there any changes that you could envisage in terms of the structure or the spend that, let's say, allow you to capture more of the profitability of DUPIXENT?

Len Schleifer

You have sort of faded out at the end. This is Len. But I think what you're asking, can we change the structure or the profitability? I think Sanofi and Regeneron are constantly looking at this. We see the same data you do. It is very early for Libtayo. So that's one thing. It's getting a little bit late for PRALUENT and KEVZARA. And we are focused on making sure we do the right thing overall for the -- so that they're not a drain on the overall alliance. You can be assured of that.

Operator

Our next question comes from Terence Flynn from Goldman Sachs.

Terence Flynn

I was just wondering, for your BCMAxCD3 bispecific, are you encouraged because you're seeing activity in a second type of cancer here with the platform or encouraged because you have a competitive efficacy profile relative to the CAR-T and ADC data we've seen from the competitors? And then any commentary you can share at a high level regarding the safety/tolerability profile at this point?

George Yancopoulos

Yes. I think that it's fair to -- I think you made two great points. I mean, I think, one, it's very important to see that the platform is consistently producing what looked like very competitive, exciting data. And so it's encouraging for that reason. And secondly, if the platform is producing competitive data in a particular area, then it's exciting for that reason as well. So I guess the answer is yes and yes on both of those.

Len Schleifer

We shouldn't go any further. We'll show you the data at ASH.

Operator

The question comes from Matthew Harrison from Morgan Stanley.

Matthew Harrison

George, I just wanted to follow up on some comments you made around C5. I guess, two parts here. So first, you mentioned a couple products that you expected at ASH, but you just said a future medical meeting for C5. Should we expect this at ASH? Or is this -- are we not going to see this at ASH? And then you also said that you're encouraged. So should we think about this as something that it looks like you plan to move into pivotal studies at this point?

George Yancopoulos

Well as I said, we had a very high bar before we would get excited about it, which was we want to feel like we could change the field. As you know, the current approaches are limited to intravenous delivery. We were looking for a subcutaneous, self-administered approach and we were also looking for more complete suppression of hemolysis. And so we are excited because we feel like we satisfied our high bar.

In terms of where we're actually going to present it, we're hoping to present it as soon as possible in a major medical conference. And so that we don't get prevented from presenting it at such conferences, we can't tell you where we're presenting. Sorry about that.

Operator

Our next question comes from Yaron Werber from Cowen.

Yaron Werber

Great. So George, maybe just one for you relating to -- give us a sense. In the Phase II high-dose EYLEA study, you're testing 8 milligrams. Can you advance that right away into the parallel Phase III pivotals? Or do you need to show sort of safety first before you can move to a pivotal and the pivotal would have a different dose?

And maybe if I can just throw in, any initial feedback on the Beovu launch that you're seeing in the last literally three weeks or so?

George Yancopoulos

I'll leave the last for Marion to comment on. But in terms of the first, of course, there's always safety concerns. But depending on whether one sees something unexpected or not, we are planning to do it exactly as you said. The Phase II is intended to simultaneously be providing data while we're running the Phase III to give us confidence that the high-dose EYLEA is actually performing and doing the things that we're predicting that it would actually do. So we're not limiting the Phase III by the Phase II data. And Marion?

Marion McCourt

Sure. And just first, we're pleased with the EYLEA performance through this third quarter and certainly been in a competitive market for some years. But specifically to the most recent launch, Novartis' launch, when you take all the important competition seriously and certainly have been prepared for new market entrants. But it is really early, so we can't report on any impact. We're not seeing any impact at this time. And I think the market will be looking to product profile to determine issues of safety, efficacy and product use.

Operator

Our next question comes from Evan Seigerman from Crédit Suisse.

Evan Seigerman

Congrats on the progress. So one for Bob. I was wondering if you could provide us some more color on the rationale for the newly announced share repurchase program. On this, this seems to be kind of a deviation from your prior capital allocation strategy. So why now? Do you believe that your share price is undervalued and that this is the best way to invest capital? Or are there other factors impacting the decision?

Robert Landry

Thanks, Evan, for the question. And again, we wanted to be kind of pointed during our script with regards to calling out the framework that we have on this because we do get a lot of questions on it. I think exactly where you kind of ended off on the question with regards to -- we currently like the valuation. Obviously, all the work we do inside here and what we know is coming and...

Len Schleifer

Bob, I got to interrupt you. I kind of hate the valuation.

Robert Landry

The valuation from a purchasing point of view is what we certainly like. Thanks for that help, Len, on that. We like the levels. And as I tried to point out, I mean, we sufficiently invest in R&D in the right areas. Things continue to move through the clinic. We are also going into external transactions. We mentioned in May the Alnylam transaction, and I

talked about a little bit that -- there on the script. So now is the right time with regards to being able to kind of put additional capital to work. And again, to reiterate what you said, we do like -- we think the valuations are attractive from our point of view at this level.

Operator

Our next question comes from Yatin Suneja from Guggenheim Partners.

Yatin Suneja

Congrats on the quarter. The question is on the lung cancer update that you provided today. I mean, if you end up with an identical result to KEYTRUDA in the front-line lung setting, do you compete on anything other than the price? Is that going to be the strategy? Could you maybe comment on the strategy there?

Len Schleifer

Yes, it's a little early to comment on a strategy till we see the data. I just remind you, this is going to be a very large space. KEYTRUDA is annualizing right now at about, I think, $12 billion. And the whole space is predicted to go much larger than that with most of the sales, at least initially, coming in lung cancer.

We have two strategies I think that George has been articulating for years. One is we need a foundational strategy so that if it just turns out the only checkpoint inhibitor that continues to make a difference, as it has for the last 5 years in lung cancer, is a PD-1 inhibitor, we want to be there with ours and we want to compete. And we'll see how the data goes. But it could be one experiment away with either some combination, a co-stim, a bispecific or something else. And then everybody's back, loaded up in the starting gate. So this has been, I think, articulated innumerable times by George: PD-1 is a foundational technology for us in the immuno-oncology space, lung cancer is the biggest opportunity, we want to be there.

Operator

Our next question comes from Cory Kasimov from JPMorgan.

Matthew Holt

This is Matthew on for Cory. So my question is on your BCMA bispecific programs. Can you talk about the differences between REGN5459 and 5458? What informed your decision to advance the former into the clinic? And whether this was in any way dependent on the initial 5458 clinical data.

George Yancopoulos

Yes. I mean, these are all great questions. I think the important point to make is, and it was brought up by a previous caller, that we are really validating our platform and we're excited that it looks like the platform works. And what we're beginning to understand is that one way to control, not only efficacy but also safety, is by the components that are used, particularly the constant components in our platform. I'll remind you, they're all created from entirely natural sequences of antibodies and so forth, so there's no immunogenicity problems.

And so what we're doing, we committed not based on any data that we saw, but to test a couple of variants of the constant aspects of the platform to try to optimize the efficacy and safety profile. Though obviously we're seeing what look like very competitive profiles right now, we're always aspiring to even do better. So it's just a matter of building and optimizing our platform to maximize the efficacy, the safety equation as best as we can and learn that -- how we can take the platform and generalize it and optimize it to the best. And that's why we're testing, in some cases, at least two versions of related bispecifics.

Len Schleifer

So let me just repeat what George said, maybe in my words, is that the platform is powerful, and therefore the activation energy to try more than one thing is low. And so we have that as a competitive advantage.

Justin Holko

Thank you. I think we have one more -- time for one more question, Sheryl.

Operator

Our final question comes from Josh Schimmer from Evercore.

Joshua Schimmer

It looks like the sequential quarter-over-quarter growth of DUPIXENT in the third quarter was much lower than it was in the second quarter despite very strong underlying prescription trends. Can you discuss some of the factors underlying that, including potential inventory or gross to net fluctuations or any other factors that might have contributed?

Len Schleifer

Josh, Marion will take that.

Marion McCourt

Sure, happy to. So Josh, we're very pleased with the quarter-on-quarter performance. And as I mentioned in my script, when we just look at, obviously the percentage growth of TRxs quarter-over-quarter, and I believe it was 21%, it was quite substantial. As it relates to gross to net and inventory, I know that inventory is within the normal range and therefore don't have more to report on that area.

Justin Holko

Great. Thank you, everybody, for joining the call. We'll be around to take questions.

Len Schleifer

Thanks a lot.

Operator

Thank you. Ladies and gentlemen, this concludes our conference for this morning. Thank you for your participation. You may now disconnect.