REFINITIV STREETEVENTS

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OVERVIEW:

Company provided an update on progress across oncology development pipeline

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PRESENTATION

Operator

Good day, and thank you for standing by, and welcome to the Regeneron Pharmaceuticals ESMO 2024 investor conference call. My name is Kevin, and I'll be your operator for today's call. (Operator Instructions) Please note this conference is being recorded.

I would now like to turn the call over to Mark Hudson, Director of Investor Relations. You may begin.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thank you, Kevin. Morning. Good afternoon and good evening to everyone listening around the globe. Welcome to our ESMO 2024 investor call. I'd like to remind you that remarks made on this call today include forward-looking statements about Regeneron's business and research and development programs, anticipated milestones and regulatory matters.

Each forward-looking statement is subject to risks and uncertainties that could cause the 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 SEC filings. Regeneron does not undertake any obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Joining me today are Dr. George Yancopoulos, Board Co-chair, Co-founder, President and Chief Scientific Officer; Dr. Izzy Lowy, Senior Vice President, translational and clinical sciences oncology; Dr. Andres Sirulnik, Senior Vice President, Hematology Clinical Development; and Justin Holko, Senior Vice President, Global Oncology and Hematology Commercial.

On today's call, George will provide an overview of our progress toward becoming a global oncology leader and Regeneron's differentiated discovery and development approach, which has generated a pipeline of novel targets across solid and hematologic cancers. Izzy and Andres will then provide select updates across our clinical pipeline, highlighting data presented across oncology programs in 2024 and outlining the path forward for a robust oncology pipeline.

Finally, Justin will provide an update on the Libtayo commercial performance and the ongoing buildout of our global commercial organization. After our prepared remarks, we'll open up the call for Q&A. I'll pass along the call now to George. George?

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

Thank you, Mark, and thanks, everyone, for joining today's call. Our overall oncology strategy is primarily focused on using the body's immune system to fight cancer. Using our deep understanding of human genetics and the immune system, together with a variety of our pioneering technology platforms, we have internally developed and clinically validated multiple independent classes of immune-oncology agents with each class modulating the immune system in slightly different ways, enabling combinations that could augment antitumor activity.

Our checkpoint inhibitors, including our PD-1 antibody Libtayo or cemiplimab and our LAG-3 antibody Fianlimab are designed to overcome T-cell suppression, thereby empowering T-cell to kill tumors. Our CD3 Bispecifics bridge T-cells to tumors, enabling the T-cells to kill the cancer cells. Regeneron has been a pioneer in this class being the first group to treat patients with a full-length, fully human CD3 bispecific.

We now have a growing pipeline of CD3 bispecifics for solid and hematologic cancers with our most advanced programs in the regulatory stages. Our CD20 by CD3 bispecific, also known as Odronextamab was recently approved in Europe under the brand name Ordspono for follicular lymphoma and for diffuse large B-cell lymphoma. And our BCMA by CD3 bispecific or Linvoseltamab, which is currently under FDA and EMA review for multiple myeloma.

Finally, our third class of clinical agents are our co-stimulatory bispecifics, which currently has four programs in the clinic and more soon to enter, designed to enhance antitumor activity when combined with either our checkpoint inhibitors or our CD3 Bispecifics. Regeneron was also the first to introduce co-stimulatory Bispecifics to treat patients.

Formation of Regeneron Cell Medicines following our April 2024 acquisition of 2seventy bio's pipeline of cell therapies complements Regeneron's pipeline of immuno-oncology antibodies, allowing us to develop potentially transformative combinations. And beyond that, we will soon start clinical investigations of additional classes of immunomodulatory therapies, including our targeted cytokines.

Next slide. It's the unique flexibility of our pipeline that differentiates our oncology approach. Our immuno-oncology efforts were prospectively designed so that the various individual agents could be rationally combined with the goal of maximizing antitumor response, resulting in a very broad and multifaceted portfolio of combinations.

And these are the programs that we'll highlight today. The innovative oncology assets in clinical development at Regeneron comprise nearly half of our pipeline across over 30 solid and blood cancers. These almost entirely homegrown assets enable us to devise rational investigational combinations, which we believe give us the opportunity to change the treatment of cancer.

With that, I'll turn it over to Izzy Lowy.

Izzy Lowy - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Oncology

Thank you, George. And greetings to everyone on the call, the rest of us are here in Barcelona at ESMO, where we've been showing our data and meeting with investigators and having a lot of excitement. I'd like to turn to our pipeline, next slide.

So Libtayo is has provided for us a best-in-class foundation for combination with other oncology assets. It was first approved by the FDA in 2018 for Advanced Cutaneous Squamous Cell Carcinoma and it is the first antibody that was approved in this indication. And following that also in Basal Cell Carcinoma, where we have established the leading presence in treatment of non-melanoma skin cancers.

We've demonstrated a commitment to this area with an adjuvant program underway that will be reading out an interim analysis by the end of this year. And we also presented a year ago practice-changing data in the Neoadjuvant setting, where our approach to giving Neoadjuvant Libtayo in patients with operable cutaneous squamous cell carcinoma has become a new standard of care.

We have also developed and gotten approval for Libtayo in lung cancer. And we are [one of two] PD-L1 or PD-1 agents that have approval in the first line setting as both a monotherapy or in combination with chemotherapy across squamous and non-squamous histologies.

At World Lung Cancer on the next slide, at World Lung Cancer, just before ESMO, we were able to present our 5-year long term survival benefit from our first approval study of monotherapy of Libtayo versus chemotherapy from the EMPOWER-Lung study. And it evaluated Libtayo as a first-line treatment for adults with either squamous or non-squamous advanced non-small cell lung cancer with elevated greater than 50% PD-L1 expression.

The presentation was a late-breaking presentation that showed that Libtayo, monotherapy nearly doubled the median overall survival and reduce the risk of death by 41% compared to chemotherapy. The median survival of 26 months, double that of 13 months. And the five-year survival rate also doubling at 30% versus 15%.

Next slide. The five-year outcome data compares favorable in cross-trial comparisons to other PD-1 or PD-L1 antibodies and further supports our position for this to be a backbone for our oncology portfolio. In this slide, we show that the data that we saw at our one-year analysis remain consistent at our five-year analysis with hazard ratios being preserved and with confidence intervals contracting as our precision around the measurements increase and the duration of our response also became as long as 24 months with the longer follow up.

In this study, we also developed new important data to help doctors manage patients in the first line setting when they're facing a choice of either giving monotherapy or monotherapy in combination with chemotherapy. We showed in a non-randomized way that patients who started with monotherapy and then subsequently progressed, could achieve a benefit by the addition of chemotherapy with preserve treatment with Libtayo offering some confidence to providers that they are not missing out by choosing to give monotherapy upfront. And this study is one of the few trials to evaluate this in a prospective way.

In conclusion, Libtayo's maturing clinical profile across multiple cancer settings has established as a strong agent in its own right, as well as a strong foundation for our oncology portfolio.

Next slide I'd like to now turn to our work with our LAG-3 inhibitor, Fianlimab. While PD-1 -- the introduction of PD-1 has been an amazing progression in the field, obviously, there's a lot of work that needs to be done to further improve efficacy even in the tumors that respond and certainly in the tumors that don't. And we worked very hard to figure out what we could add to cemiplimab (technical difficulty) in our early clinical data in metastatic melanoma suggested that LAG-3 blockade with Fianlimab plus cemiplimab might be an unusual combination that would demonstrate meaningful additive benefit and without the cost of exacerbating safety.

At this ESMO conference, we presented new two-year results evaluating the combination of Fianlimab and Libtayo in adults with advanced melanoma pooling three independent expansion cohorts from our first-in-human multi-cohort study. The combination is being further studied in an ongoing randomized Phase 3 study of Fianlimab and Libtayo versus pembrolizumab monotherapy in previously untreated unresectable locally advanced or metastatic melanoma. This pivotal study has been enrolling briskly and is expected to readout sometime next year.

In addition, we are also -- in melanoma studying the utility of Fianlimab and cemiplimab in the adjuvant setting and in the perioperative setting. And we have also mounted a study comparing in first-line metastatic melanoma head-to-head against the current standard of care approved PD-1 LAG-3 combination to demonstrate that our combination is at least as good, if not superior to what's out there.

Next slide. With longer follow up of the initial cohorts, Fianlimab and Libtayo continue to demonstrate encouraging antitumor activity in advanced melanoma patients. Now with a median follow-up of 23 months and a median treatment duration of 35 weeks. The results show persistent and deepening tumor responses across all three independent cohorts. And you can see in the pooled analysis, the last column on the right of the table, that our objective response rate overall is 57% and including a development of a 25% complete response rate, 24 of 98 patients.

This complete response rate has evolved and emerged over time when our earlier cuts, it was more on the order of 12% to 15%. And in fact, it is this durability, as highlighted on the next slide, where you can see the spider plots showing the -- Next slide please. Showing that the -- benefits,

once they occur are rock solid and persist out well beyond the treatment duration, even in patients with stable disease. And this actually has emerged as a theme that we see in our experience with this combination that patients once they respond appears to develop durable responses.

Robust clinical activity was observed also in subpopulations where one might expect weaker results, and there is currently no established standard of care such as patients who were previously treated with anti-PD-1 in the adjuvants or the neoadjuvant setting. Here, 6 out of 13 patients who had previously been treated with PD-1 in that setting responded to therapy for an ORR of 46%. And overall, anyone who had had any type of adjuvant [or neoadjuvant systemic therapy,]11 out of 23 also close to 50% had benefit from the combination.

The safety profile on the next slide showed that the combination was generally well tolerated, consistent with the safety profile of Libtayo monotherapy and other PD-1 agents. The one notable exception was a slightly higher rate of adrenal insufficiency with 12% of patients, of which 5% were at grade three. What was striking was in those 12 patients who had the adrenal insufficiency, we had a 92% overall response rate, suggesting that there is something linked between that particular adverse event and efficacy.

Overall, adverse events of any grade occurred in 95% of patients. Grade three or greater or immune mediated adverse events were in 47% and high grade were 13%. AEs leading to death occurred in seven patients, two were considered treatment related.

On the next slide, we show some cross trial comparisons understanding the caveats of such comparisons. But as you can see, based on the preliminary proof of concept data from the three independent cohorts that we presented with long term follow up, we have nearly doubled the complete response rate compared to other PD-1 monotherapies.

We have a median PFS of 24 months, which significantly outperforms other treatments in patients with similar baseline characteristics and this durability and safety gives us confidence [in the profile of this combination] for advanced melanoma and potentially other cancer indications. Amongst the various trials that we are pursuing, we have two lung cancer trials that in Phase 2, that one of which should be reading out by the end of this year in combination with chemotherapy.

And the next slide shows some data that we presented at ASCO, suggesting that we had an elevated response rate compared to monotherapy in head and neck squamous cell carcinoma, again with a durable response lasting for as long as 20 months as a median. And therefore, we have also decided to initiate a trial in both HPV-positive and HPV-negative first-line head and neck squamous cell carcinoma in patients who are PD-L1 positive.

So next slide. In conclusion, our long-term follow-up of advanced melanoma patients treated with the combination have shown encouraging and very competitive response rates and PFS across three independent cohorts. This combination may offer a potential best-in-class treatment in first-line metastatic melanoma, which we will learn with the pending Phase 3 results next year. We have encouraging results that we've seen in head and neck squamous cell carcinoma and therefore initiating a randomized Phase 2.

And our studies in lung cancer will also readout and we are initiating potentially pivotal Phase 2 studies for Fianlimab and Libtayo in perioperative melanoma, and in perioperative lung cancer.

Next steps. We have the results from our Phase 2 studies in lung cancer later this year and hopefully be able to present registration enabling data from the Phase 3 study sometime next year from melanoma.

Next slide. So let's turn back now to our Costims. So as George mentioned, we were actually the first to initiate these types of molecules in the clinic where on the basis of preclinical data, we realized that the CD28 pathway was a potent lever to employ, to augment immune responses and essentially tried to convert tumor cells into antigen-presenting cells. And what you can see here is the example of the mechanism, how we see these working, where a costimulatory bispecific bridges CD28 to a tumor associated antigen rather than the CD28 engaging its normal B7 ligand, which then in combination with anti-PD-1 can augment un-normal signal that the TCR recognize.

Regeneron's first in class CD28 Costim, which was a PSMA by CD28, demonstrated proof of concept for this mechanism in which we saw rapid and dramatic responses in prostate cancer with three or four patients dropping significantly with their PSA, although it was complicated by immune mediated adverse events.

Therefore, we have taken on the next [slide,] steps to further augment our ability to separate the efficacy from any safety issues. And we are doing this in a number of different ways. We are testing monotherapy cohorts with an option to add lower dose cemiplimab if there is no response, we're also investigating the combination of our prostate-specific costimulatory bispecific with a CD3 bispecific, which based on strong preclinical data, we believe will be better tolerated and may provide a similar efficacy profile, and we are exploring additional approaches to prostate cancer utilizing our CD28 platform, which are being evaluated preclinically.

Next slide. We have made the decision to test this co-stimulatory bispecific platform in multiple different settings. In currently exploring them in early clinical trials across a variety of solid and hematologic tumor settings in combination with cemiplimab or in combination with complementary CD3 bispecifics with more to enter the clinic soon.

I'd like to next focus on our EGFR by CD28, where we presented initial dose escalation data in microsatellite stable colorectal cancer at ASCO earlier this year. That's another cancer that is typically viewed as unresponsive to PD-1 monotherapy or has failed other combinations with chemotherapy to date.

Next slide. At ASCO, we showed that in our dose escalation study in a cohort of 15 patients who had advanced colorectal cancer, but without liver metastases, 3 out of 15 or 20% had a significant response rate and 80% showed disease control rate. Microsatellite stable colorectal cancer historically has been unresponsive to immunotherapy and these early results in combination with Libtayo are encouraging, again showing that the antitumor responses in a highly difficult to treat cancer can be obtained and we are working now to explore the ability of this in multiple other treatment settings in different indications.

As you can see from the bottom on the right, safety was assessed in 84 patients with multiple solid tumor types at a variety of doses. The combination showed an acceptable safety profile, and the maximum tolerated dose has not yet been reached. There have been no dose-limiting toxicities to date and notably no reports of cytokine release and no treatment related deaths. Of particular note, we have not observed the same type of severe immune mediated adverse events through the dose level that we've reached so far of 900 milligrams as have been seen with PSMA by CD28, indicating to us that there is much to learn about this whole class of agents and that each one may have slightly different properties, and we are working hard to learn the rules for how to optimally use these.

We are now in opening up additional [expansion cohorts for the] combination, including patients with lung cancer, head and neck squamous cell carcinoma, cutaneous squamous cell carcinoma as well as more patients with colorectal cancer.

Next slide. So our conclusions on the Costim bispecific platform, we are focused on developing a unique portfolio of oncology medicines, including checkpoint inhibitors, CD3 bispecifics and CD28 co-stimulatory bispecifics. Not mentioning here, the cytokine directed therapies, potential for cellular therapies and other combinations that we're doing -- that we're developing preclinically and in collaboration with other companies.

Over the past several years, we've made progress in our programs across checkpoint inhibitors and the CD3 class and are now showing promising activity with two co-stimulatory bispecific antibodies in the clinic. These were designed with the goal of turning cancer cells into antigen-presenting cells, thereby converting historically immunotherapy unresponsive tumors from cold to hot.

Early data speak to the potential of EGFR by CD28 in combination with Libtayo and add to a growing body of evidence supporting novel co-stimulatory bispecifics that are in clinical trials for a range of both solid and blood cancers and turning to blood cancers, I'll turn now to Andres to carry on

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Hematology

Thank you, Izzy. I will now discuss the recent progress and updates across our hematology oncology development pipeline, focusing on linvoseltamab, our BCMA by CD3 antibody for myeloma and Ordspono, our CD20 by CD3 [antibody] was recently approved in Europe for [certain] lymphomas.

Next slide, please. I will start with linvoseltamab, at the recent European Hematology Association Congress, we presented 14 months median follow-up data from the ongoing LINKER-MM1 trial in patients with relapse refractory multiple myeloma. As a reminder, an earlier data cut at 11 months serve as the basis for regulatory filings in both US and Europe. These longer-term data further reinforce our confidence in linvoseltamab as a potential best-in-class BCMA bispecific. And we are continuing development in earlier lines of therapy.

Last month, we announced that the FDA had issued a Complete Response Letter for the BLA in the relapsed refractory setting related to findings from a pre-approval inspection at a third-party fill finish manufacturer for another company's product candidate. We are working with all stakeholders to resolve this issue. The third party manufacturer is awaiting for inspection by the FDA, which is expected to take place in the coming months. In Europe, we anticipate a regulatory decision by the first half of 2025.

And now let's move to the data on the next slide. linvoseltamab demonstrate deep and durable responses in patients with relapsed refractory multiple myeloma. As the graph depicts, we continue to see a trend of responses deepening over time. Based on the latest data cut with a median follow-up of 14 months, a 71% objective response rate was observed in patients treated at 200 milligram dose. This was assessed by an independent review committee also showing 50% of patients achieving a complete response or better. This response rate and complete response rates continue to represent a highest rate across the BCMA bispecific class.

Next slide, please. As we previously highlighted, responses occur early, deepen with time and have shown durability, all critical efficacy measures for this heavily pretreated patient population. Based on the 14 month a median follow-up, the median duration of response was 29 months for all responders. While the median duration of response had not been reached for those who achieved a complete response or better.

Now turning to safety briefly on the next slide. Linvoseltamab show a manageable safety profile that was generally consistent with the early data cut, and it is important to emphasize that the majority of patients did not develop CRS. CRS was reported in 46% of the patients, and most of those were Grade 1. There was one Grade 3 CRS event during step-up dosing, but no other Grade 3 or higher CRS events were observed. And these CRS events mostly occur during the step-up dosing period and typically occur and resolve within 24 hours.

Next slide, please. Based on clinical evidence to date, we believe linvoseltamab has a compelling and differentiated profile relative to other FDA approved BCMA bispecifics. Of course, we should take into consideration that these are comparisons across different trials. But with that caveat, we can state that we have a compelling differentiated BCMA bispecifics. While the 11 month data cuts serve as the basis for our regulatory filings, the updated data further supports a potentially best-in-class profile for linvoseltamab in late-line myeloma in terms of efficacy, safety [and dosing and patient burden].

Next slide, please. We are rapidly advancing our clinical development program into earlier lines of therapy, including premalignant conditions. And given the strength of the data in late lines of therapy, including the extra level of efficacy and favorable safety profile of linvo, we are exploring monotherapy approaches in early lines of therapy as well as novel combinations.

In the context of early lines of therapy, we look to expedite our trials by incorporating MRD endpoints that could accelerate development. We are also evaluating linvoseltamab in precursor conditions such as smoldering myeloma and Monoclonal gammopathy of unknown significance or MGUS while study in Amyloidosis is also enrolling. These indications represent potential opportunity for linvo to help even more patients in need.

In summary, I believe linvoseltamab is among one of the most exciting programs that we have in our clinical pipeline, and we are rapidly advancing development efforts to bring this important therapy to many more patients.

Next slide, please. Moving now to odronextamab, which now has the brand name of Ordspono. This is our CD20 by CD3 bispecific antibody in lymphoma. Ordspono, which was approved in Europe last month is Regeneron's first bispecific approval. It is approved in both relapsed refractory follicular lymphoma and relapsed refractory diffuse large B-cell lymphoma.

We know that the EU label Ordspono can be administered in the outpatient setting and does not have hospitalization requirment. As we previously highlighted, Ordspono has the highest complete response rate in the setting of follicular lymphoma and for diffuse large B cell lymphoma is the only bispecific in the class to have a post-CAR-T cohort in its label, high [unmet need]. We continue to enroll patients in Phase 3 confirmatory trials, and will provide further updates later this year on progress made on the FDA regulatory front.

Next slide, please. You can see that we have a comprehensive OLYMPIA development clinical program for Ordspono, which is progressing rapidly. We are enrolling across several Phase 3 studies evaluating [Odro], both as monotherapy and with novel combinations to challenge the current treatment paradigms. We are also very excited about progressing a combination of CD28 costimulatory bispecific with Ordspono. We are hopeful to increase activity in late lines of therapy and beyond.

In summary, we are excited about the prospects of odronextamab in lymphoma and the progress that we are currently making across the entire clinical development program.

Next slide. To summarize, Linvoseltamab demonstrated potential best-in-class efficacy, and we believe it is highly differentiated from the competition. Ordspono continues to show durable responses and a competitive profile with a recent approval in the EU. And based on the competitive and differentiated profiles of these bispecifics, we are pursuing a large clinical development program in earlier lines of therapy with a goal of establishing Regeneron as a leader in hemato-oncology.

With that, I will turn to Justin.

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Global Oncology and Hematology Commercial Business Unit

Thank you, Andres. Izzy and Andreas have reviewed exciting data from across the oncology portfolio and now I'd like to speak briefly about the ongoing build-out of our commercial oncology organization and the success we've had with Libtayo as well as how this positions us for long-term success as the pipeline continues to mature.

Next slide, please. Since the initial launch of Libtayo in cutaneous squamous cell carcinoma in [2018], we have [executed] commercially to establish the brand as the leader in this disease category with approximately 80% share of the PD-1 class. And we continue to make tremendous progress on growing this market given the significant unmet medical need that is out there.

With the addition of basal cell carcinoma, we have solidified Libtayo as the leading anti-PD-1 therapy in non-melanoma skin cancers. Despite increasing competition in recent years. Libtayo growth has also been fueled by the approval in non-small cell lung cancer, where in 2022, Libtayo became one of only two PD-1 antibodies to be approved in the US for use in the first-line setting in combination with chemotherapy, irrespective of histology or PD-L1 expression level.

We have steadily grown Libtayo's share in both monotherapy and with the chemotherapy combination despite entrenched competition. In the first half of 2024, Libtayo global net sales grew 43% to $561 million, putting Libtayo on track to be Regeneron's next drug to surpass $1 billion in annual net sales and with significant margin expansion over the last couple of years.

Next slide, please. Our acquisition of global rights to Libtayo from Sanofi in 2022 has provided us with the opportunity to expand our international commercial presence to support the strong growth of Libtayo. As of July, we have completely transitioned the Libtayo business from Sanofi. We have attracted an all-star team from a diverse set of backgrounds with strong oncology and hematology expertise. Our international operating model is also designed to support launches in hematology and potential future treatments.

Speaking of hematology, we are pleased about the recent approval for Ordspono in Europe, and we look forward to a decision from regulators [in Europe on linvoseltamab] in the first half of 2025. In the US, our hematology oncology commercial teams are well prepared to begin launch activities for both treatments pending resolution of the complete response letters, which were received from the FDA.

In summary, our organization has driven strong growth for Libtayo through solid commercial execution. We have expanded our global footprint across international markets, and we are well positioned to maximize both Libtayo and future brands in oncology and hematology.

I'll now turn the call back over to George for some closing remarks.

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

Well, thanks, Justin. As I hope you've all heard from Izzy and Andres and Justin, that there's been a lot of exciting developments with our innovative pipeline. I think some, of course, things just to emphasize again, as Izzy said, first of all, in terms of our work with checkpoint inhibitors, he presented perhaps some of the most exciting new data since the dawn of the checkpoint inhibitor era in terms of new combinations with new abilities to take these classes of agents to the next level and showed incredibly striking data, particularly if you focus on things like the complete response rates and the durability that Izzy described.

Similarly, Andres talked about our innovative class CD3 bispecifics and once again, perhaps best-in-class data for the very important BCMA class of CD3 bispecifics, once again with perhaps a field leading data in terms of very importantly, complete responses and duration of action for patients suffering from this very serious disease and a recurring theme from both Izzy and Andres was the flexibility based on the many modalities we have in our pipeline of prospectively and logically designing combinations that can take activity to the next level, not only with the combinations that I just mentioned, but also, for example, with these very innovative costimulatory bispecific approaches that they talked about.

And of course, Justin finish by talking about how we're moving forward and doing well commercially and particularly with our first checkpoint inhibitor as a monotherapy, as you said, on its way to becoming a $1 billion drug. But just as importantly, that's as a monotherapy that's not talking about what the possibilities in the future can be as it's going to be a foundational agent for a variety of our ongoing and future combination approaches.

So with that summary, I'll turn it over to Mark to take questions.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thank you. We'll now open the call for Q&A where George, Izzy, Andres and Justin can address your questions. In order to address as many questions as possible, we ask each caller to limit themselves to one question and please keep the scope of your question limited today's subject matter.

Kevin, please go ahead.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Evan Seigerman, BMO Capital Markets.

Unidentified Participant

And this is Connor on for Evan. And thanks for taking our question and congrats on all the data. With data from the Phase 2 Fianlimab plus Libtayo front-line lung study coming in the fourth quarter. Can you maybe just share what you view as the bar for that readout to take it into Phase 3? And then maybe any read-throughs or potential points of differentiation from the Opdualag data that we saw this weekend? Thank you.

Izzy Lowy - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Oncology

Hi Evan. So one of the things we were pleased about to see in the Opdualag data was additional data emerging that LAG-3 can augment the responses in lung cancer to PD-1 and chemotherapy. We believe we have the opportunity to do better than that. But I think we will have to see what the data reads out as. We have a stronger PD-1 chemo combination performance in first-line lung cancer than the control arm in that study of [nivo plus chemo].

And we have, as you know, from our what we shared in melanoma, we believe we have competitive performance of the combination of LAG-3 of Fianlimab and cemiplimab and I'm not going to predict the specific criteria, we have to be convinced that we are seeing a clear benefit in the first-line lung cancer setting in order for us to take it forward.

Our initial data was with a limited cohort where we saw a -- again what looked like an enhanced response rate, but more compelling to us was the durability that we saw. So that's going to be the kind of the general criteria (technical difficulty) deeper responses and the opportunity for suggesting that they will be more durable, although we obviously won't have as much follow up.

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

Thanks Izzy. Let me just add and amplify a little bit to that. So as Izzy said in the BMS data, they seem to show a small dataset that the LAG-3 blockade added to the activity of their PD-1 agent, [Nivolumab]. But it's important to point out that in their study just as in all their historical studies, nivolumab under performed other PD-1s, most notably in lung cancer, as we know our PD-1 agent Libtayo that you just heard about as well as Keytruda have the class leading data and that nivolumab has not been approved as a monotherapy or as a single agent on top of chemo because it just doesn't look as powerful an agent in lung cancer.

That said, in their small study, the LAG-3 added to that. So Izzy points out that if you would now have a more powerful PD-1 and perhaps a more powerful LAG-3 approach, which looking at the data right now, there is a real opportunity that we would have it that we could have profoundly more exciting data, and that's what we're hoping for. And as Izzy said, we're hoping when we see the data that will be clear cut and it will point to a direction that we'll want to undertake in lung cancer.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thank you. Kevin let's go to the next question.

Operator

Tyler Van Buren, TD Cowen.

Tyler Van Buren - TD Cowen - Analyst

Hey, guys. Thanks very much for the presentations. You guys are doing a lot of great work in oncology. So I wanted to ask about Fianlimab again, given the data of Fianlimab and Libtayo melanoma, I'd be shocked if the Phase 3 next year was not successful. So perhaps we could talk about the

market a bit. What percent of the frontline melanoma market, do you believe a LAG-3 I-O combo could take and do observations with the ongoing Opdualag launch support that so far?

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

Why don't we let Justin take that.

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Global Oncology and Hematology Commercial Business Unit

Thanks for the question, Tyler. When it comes to oncology, physicians -- treating physicians really look at the data. And if we can deliver unambiguous promotable differentiation, that's something that is going to resonate with customers. We see with the current agents on the market that there is already some pretty strong uptake. So our expectation is that if we can deliver on what we're seeing in the Phase 2 cohort that it could be a significant opportunity for us in first-line melanoma.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thanks, Justin. Kevin let's go to the next question.

Operator

Salveen Richter, Goldman Sachs.

Unidentified Participant

Hey, good morning and thank you for taking our questions. This is Elizabeth on for Salveen. Wondering if you could help contextualize and kind of remind us of the discontinuation rate for the Fianlimab study in melanoma for the data that was just presented at ESMO and kind of what are some contributing factors to the discontinuation seen.

And then second question also on Fianlimab, if you could speak to the relative importance of LAG-3 expression in patients with non-small cell lung cancer. And if there's any expression criteria for the Phase 2, 3 study and that we'll see data from later this year. Than you.

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

Well, Izzy why don't we let you take the question, if you can put the slide back on that shows [the spaghetti plot] that shows durability that Izzy had highlighted. And then Izzy, you can maybe take on the question about discontinuations first.

Izzy Lowy - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Oncology

So the overall discontinuation rate was in the (inaudibe) that were discontinued due to treatment-emergent adverse events was about 17% -- 17 patients out of 98. The main if you look across different trials, the overall discontinuation rates were similar to what's been seen in other advanced cancer settings, where generally it was due to either progressive disease or it was due to actually patients deciding that they had good responses and no longer wanted to continue treatment.

So I think those were basically on par. What you see here on the spider plots is the durability of responses that actually could encourage physicians and patients to say that they would stop. I'll point out that this first in-human cohorts are originally planned only a year of therapy rather than the typical two-year therapy that we have in our Phase 3 program.

And so only a proportion of patients actually decided to opt for an optional second year. And what we didn't show on the slides here, although it's listed in the subheading, we did look at PD-L1 or LAG-3 expression in the melanoma group. And we did not see a marked difference between an activity in the high PD-L1 versus low PD-L1 or high LAG-3 and low LAG-3. It's important to know the two measurements are a little confounded, they're not independent because it's usually patients who have higher PD-L1 expression that might be more likely to have higher LAG-3 expression.

So we see important -- there's a slightly higher response rate and the high PD-L1, LAG-3 goes up to closer to 70%, whereas it goes in the mid 50s. If it's on the lower PD-L1. But within the context of this study, we didn't think it really differentiated. And in fact, in our Phase 3 program, we are not requiring a specific PD-L1 or LAG-3 expression level.

Similarly, in our Phase 2 lung cancer cohorts, what we're doing is we're doing one Phase two study for patients with PD-L1 greater than 50%. Where we're testing the combination of cemi versus semi and Fianlimab as an I-O/I-O combination. And then we're also testing the combination of PDL-1 -- PD-1 cemiplimab plus Fianlimab on top of chemotherapy across all PD-L1 levels. At this point, we are not predefining a particular cutoff required for looking for activity. We want to see what we get first, and then we'll learn from that.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thank you, Izzy. Kevin let's go to the next question, please.

Operator

Chris Schott, JPMorgan.

Chris Schott - JPMorgan - Analyst

Great. Thanks so much. Just maybe pivoting over to the BCMA bispecific, can you just elaborate how you are you thinking about competitive dynamics here over time? Seems like some of your competitors are evolving their dosing profiles. I'm just wondering just your thoughts on -- do we end up with the various [products on this] market end up with dosing and hospitalization that maybe looks more similar when different to one another. And how do you think about that would mean competitively? Thank you.

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

Why don't we put up that slide that shows the various agents. And Andres, why don't you take that question?

Andres Sirulnik - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Hematology

Thank you for the question. So in terms of how we see Linvoseltamab -- first, I want to start with at the level of efficacy that we have upside, which I believe is very competitive. I want to remind you, 71% overall response rate and a 50% CR rate which are very durable and I think does a rather remarkable in this difficult to treat patient population that actually was included in our pivotal clinical trial. So that's one aspect.

I think that the other important aspect that differentiating Linvoseltamab from others is as mentioned the dosing regimen. It has a convenient dosing regimen with minimum hospitalization. In addition to that the fact that the schedule of administration is a competitive. This is the only in the class of bispecific targeting BCMA that eventually has been explored given every four weeks.

Again, for those patients that achieved a VGPR better, we extended the interval of administration to every four weeks initially once a week, then types of week and eventually to every four weeks. And this is the only one that has been at the moment prospectively studied in that manner.

So all in all, I think that the data that is emerging, it consolidates (technical difficulty) we have a competitive BCMA bispecific.

Justin Holko - Regeneron Pharmaceuticals Inc - Senior Vice President, Global Oncology and Hematology Commercial Business Unit

Like the other thing I would add to this is that when you look at the BCMA market, particularly in relapsed refractory settings, it's a very fractionated market. And you think about multiple modalities. You have CAR-Ts, you've got on ADC's drug conjugates, antibody drug conjugates. You've got bispecifics. We expect that the bispecifics class is going to grow over time, just given the convenience, given the strength of the data, some of these other drugs have limited durability, some of these other classes have toxicity and other challenges. So not only, as Andres said, does our data really hold up within the class, but we expect this class is going to grow over time.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Great. Thank you. Kevin let's go to next question.

Operator

Brian Abrahams, RBC.

Unidentified Participant

Hi. This is Joe on for Brian. Thanks for taking my question. And so back to melanoma, can you talk more about adrenal insufficiency events you saw, how they were typically managed and how transient or persistent these events were. Thank you.

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

Izzy, why don't you take that?

Izzy Lowy - Regeneron Pharmaceuticals Inc - Senior Vice President, Translational and Clinical Sciences, Oncology

So on the safety slide, which is slide 17, we pointed out that there were a 12% rate of any grade of adrenal insufficiency and 5% that were Grade 3 or greater. I would point out that no one died because of this and number two, that patients were able to continue treatment with replacement steroids. And as I also pointed out remarkably that the response rate in these patients was actually 92%.

Again, it's a small subset of the group, but it suggests that there was something interesting linking this toxicity. Also point that in cross-study comparisons with other LAG-3 antibodies, it's not that dissimilar. So I think there's something about the LAG-3 targeting access that has uncovered a propensity towards a higher rate of adrenal insufficiency, still not completely clear how much of this is primary adrenal insufficiency versus secondary adrenal insufficiency coming from a pituitary source, but it's manageable. And in our studies so far our investigators, say well compared to PD-1 and CTLA-4, this is a walk in the park activity.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thank Izzy. Kevin let's go to one more question, please.

Operator

Terence Flynn, Morgan Stanley.

Terence Flynn - Morgan Stanley - Analyst

Great. Thanks for taking the question, and thanks for the overview. Obviously, there's been a lot of excitement over the last several months on PD-1 VEGF bispecifics. I know you guys have a different type of bispecific platform, but just wondering if that's something you've looked at all in any of your animal models, if that's something you're considering? And then what are the implications as you think about kind of future lung cancer market? Thank you.

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

Yeah. I was going to just make comments. Certainly, the reported data looks very interesting. It's a completely different class of bispecific. Right now, it's not obvious why in this case, a bispecific here would have any different sort of activity than just combining PD-1 and VEGF blockade. And there really is no good design purposes for making this type of bispecific, but it's certainly data worth keeping eye on.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Great. Thanks George. Kevin, I think we have time for one more question.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - Wells Fargo - Analyst

Thank you for squeezing me. And going back to the Opdualag data. So I just -- like what could be your rational behind that combination, not working -- less than 1% PD-1 patients. Is it down to PD-1 there? And in that regard, your combination could be better because more and more you look at the data, Libtayo seems more like [Keytruda than] any other agent that is out there.

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

It was a little hard to hear the question. Mark, Could you repeat the question, Mark, if you heard it.

Could you repeat that question, please for the rest of us in who didn't hear that well.

Mohit Bansal - Wells Fargo - Analyst

Sure. I can repeat it. So the question is for Opdualag, what would be the -- like when you look at the data, what is your internal thinking about why this drug did not work among the less than 1% PD-L1 patients. Is it down to the checkpoint inhibitor or a PD-1 inhibitor here? And to that point, do you think your combination may have a better shot at that particular subgroup of the patient, given that your PD-1 seems more similar to a Keytruda rather than nivolumab. Thank you.

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

Yeah. I think it's hard to read the tea leaves with these very small data sets right now. But I think that the big point that you're making and that Izzy I both tried to make, which is that if you're going to do a combination in lung cancer or in any setting, with the PD-1 and LAG-3, you want to have

the best possible PD-1 and you have the best possible LAG-3, and then you're putting them together, especially with the combo that looks like it might have best-in-class activity.

So I guess that's why the reason they have both hope and excitement about our combination because we believe we are doing that. We are putting a best-in-class PD-1 together with a best-in-class LAG-3 that's already has suggestive data in one setting with a rather large dataset, though, still limited in first line melanoma. And then I think increases the potential and the excitement that it could also have exciting performance and exciting benefit for patients in another setting such as lung.

But the data sets right now are a little small and hopefully will contribute to them, will contribute to the understanding, will contribute to the exciting potential for our combination particularly.

Mark Hudson - Regeneron Pharmaceuticals Inc - Director - Investor Relations

Thanks, George, and thanks, Izzy, Andres and Justin as well. And thank you, everyone, for joining -- who joined this call today. Apologies to those that we couldn't get into the queue today. We're happy to follow up after this call. I hope everyone has a great day, and thanks again for joining us.

Operator

Ladies and gentlemen, this does conclude today's presentation. You may now disconnect and have a wonderful day.
